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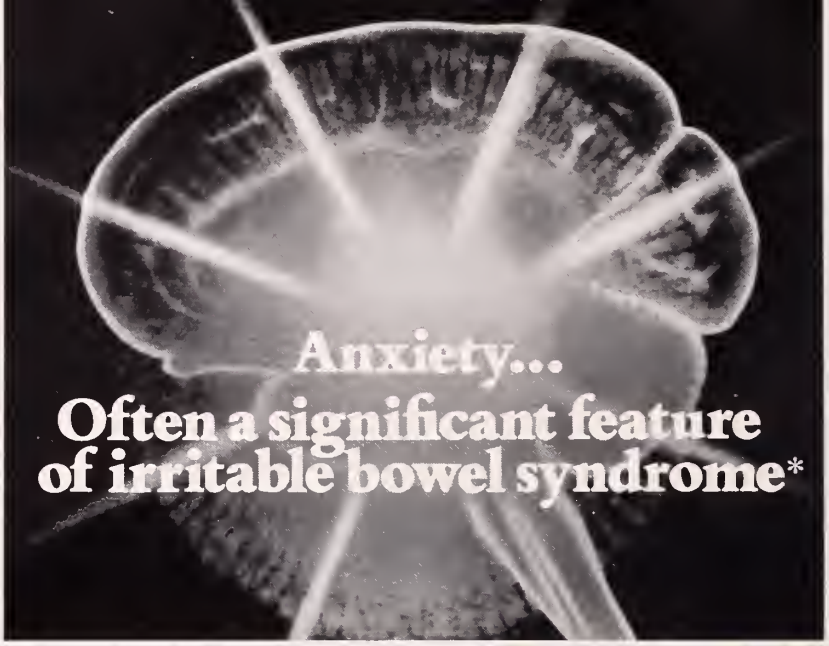

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County Society Notes

Androscoggin

The meeting of the Androscoggin County Medical Society was held at No Tomatoes on October 20, 1977.

The meeting was called to order by the President, Dr. Charles A. Hannigan, at 8:30 p.m., with 58 members and two guests present.

The minutes of the September meeting were read and approved as read.

The names of the following doctors were presented for admission to membership: Drs. Michael A. Demos, Allan M. Ingraham, Iain D. Sanderson, David D. Smith, Candace C. Walworth and Edward Z. Walworth. They were voted to membership in Androscoggin County Medical Society and the Maine Medical Association.

The transfers of Dr. Russell V. Radcliffe from Penobscot County and that of Dr. John F. Egan from Oxford County were approved.

The request of Dr. Robert A. Frost for transfer from active to affiliate membership was approved and recommended unanimously.

Correspondence from Mr. Bernstein and Pat Darling, the chairman of the Ad Hoc Committee, was noted and placed on file.

Dr. Charles Hannigan appointed a nominating committee: Drs. Louis A. Fishman, Gilbert A. Grimes and Gerard L. Morin. They are to present a slate of officers, five delegates and five alternate delegates, as well as a candidate for the executive committee of M.M.A., representing District VII for the years 1978-80.

Dr. Thomas F. Shields reported his finding on AMA Negotiation Seminar. A motion was made by Dr. Shields, after discussion, and duly seconded to make plans for a Negotiation Seminar in March 1978. It was voted 24 to 0 in favor.

Dr. Jou S. Tchao introduced the speakers, Dr. Manu Chatterjee and Dr. Blaisdel. Their presentation was most informative and a lively discussion ensued. Dr. I. O'Sullivan moved that the Androscoggin County Medical Society request the assistance of Dr. Chatterjee to assist in finding a director of Medical Education for Androscoggin County. The motion was duly seconded and voted. Dr. Tchao thanked the speakers for their assistance.

The meeting adjourned at 9:45 p.m.

FREDERICK B. LIDSTONE, M.D., *Secretary*

Franklin

A meeting of the Franklin County Medical Society was held on October 3, 1977.

The meeting was called to order by Dr. Paul A. Brinkman, President.

1. *Elections to Medical Societies* — The first order of business were the elections of Drs. David S. Hurst and Melissa A. Weekley to the County and State Medical Associations.

2. *Election of Officers* — A slate of the following officers was elected with single ballot:

Continued on Page 29

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Volume Sixty-nine | Brunswick, Maine, January 1978 | Number 1

Acute Interstitial Nephritis in Children — A Process Produced by Streptococcal Infection and by Chemotherapeutic Agents

A Review

JAMES E. HADDOW, M.D.* AND JAMES L. ROBOTHAM, M.D.**

Physicians who care for children are frequently unaware of the existence of acute interstitial nephritis (AIN). Despite this fact, AIN in its mild form is a frequent occurrence in children suffering from acute streptococcal infection.[1,2] A much more severe form of AIN also may occur in children, albeit much less commonly, and under these conditions the etiologic agent may be either streptococcal infection or drug therapy.[3,4,5] In the vast majority of cases renal biopsy is not warranted, since the process is both mild and self-limited. This has hampered general recognition of this entity. AIN occurs simultaneously with acute streptococcal infection and subsides as the infection goes away. In this regard and in many others it is separate and distinct by clinical, laboratory and histologic criteria from acute post-streptococcal glomerulonephritis (AGN). Table 1 summarizes the pertinent differences between the two disease processes. It is the purpose of this paper to review the subject of acute interstitial nephritis in children as related to streptococcal infection and chemotherapeutic agents so that physicians dealing with children may better understand its characteristics, course, and prognosis.

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Streptococcal-Induced Acute Interstitial Nephritis

For several decades preceding the antibiotic era, acute interstitial nephritis was a recognized complication of Beta-hemolytic streptococcal infections, the first post-mortem observation linking streptococcal infection with AIN having been made in 1860.[6] Death from streptococcal disease was not an uncommon occurrence, and there followed numerous similar observations during the succeeding 75 years. In 1936, Brody and Smith,[7] while reporting their own findings, made a very comprehensive review and summary of the literature. They concluded that streptococcal infection was very likely the only infectious agent capable of producing AIN in spite of the fact that other authors had included diphtheria and measles as etiologic agents. They pointed to their own experience and to comments of others emphasizing that even when other infections were primary, streptococci could be demonstrated as secondary invaders when interstitial nephritis was found at autopsy. They also demonstrated that neither bacteremia nor actual organ invasion was necessary for such kidney changes to take place. They proposed that a streptococcal toxin was responsible for the lesion, acknowledging that this idea was widely accepted in Europe, but not in the United States. Their own study included 44 cases of proven scarlet fever, 32 of which showed abnormal renal histology. They also surveyed the pathology files at their institution and discovered over 1000 cases of interstitial nephritis, in all of which cases the streptococcus was either the primary or second-

Table 1

	Acute Interstitial Nephritis		Acute Glomerulonephritis
Etiology	Streptococcal (? Extracellular products)	Chemotherapeutic	Streptococcal (Soluble antigen — antibody complexes)
Age Affected	All ages	Predominantly adults	Predominantly Children
Onset	Simultaneous with infection	Variable time after therapy begun	1-3 weeks after infection
Symptoms	Asymptomatic to acute renal failure	Asymptomatic to acute renal failure	Asymptomatic to acute renal failure
Hypertension	Rare without acute renal failure	Rare without acute renal failure	Frequent — even without acute renal failure
Rash	Phage-Dependent	Frequent and allergic in character	None
Urinalysis	No RBC Casts	No RBC Casts	RBC Casts
Beta-1-C Complement	Normal	Normal	Decreased
Eosinophilia	Minimal	None to striking	None
Strain Specificity	Unknown	Not applicable	Yes
Anti-streptolysin O Titre	Normal but often rising with time	Normal	Variable
Anti-DNA ase Titre	Unknown		Frequently elevated
Pathology			
(a) Glomerulus	Normal	Normal cellularity Minimal capillary change	Hypercellularity
(b) Tubules	Occasional necrotic area		Hyaline droplets in proximal tubules
(c) Interstitium	Edema, round cell infiltrates, occasional eosinophils	Edema, round cell infiltrates, occasional eosinophils	Mild edema; only rarely prominent scattered foci of polymorphonuclear and round cell infiltrates
(d) Electron microscopy	No deposits	Basement membranes — Glomeruli and tubules Dense deposits	Glomerular subepithelial dense deposits
(e) Immunofluorescence Complement Fixed	No	No	Yes
(f) Immunofluorescence IgG Fixed	No	Yes	Yes
Recurrences	Unknown	Common with re-exposure	Rare
Prognosis	Excellent	Excellent	Generally favorable — occasionally progressive

ary infecting agent. Kannerstein[8] reported further pathological cases relating AIN to streptococcal infection. Mallory and Keefer[9] described 90 cases of fatal streptococcal infection, 47 resulting from scarlet fever, 26 from erysipelas, and 17 from hemolytic streptococcal sepsis resulting either from cellulitis, puerperal infections or septic wounds. Every decade of life through the seventh was represented in their study, the greatest number of deaths occurring in the first decade. Interstitial nephritis was found in 47% of their cases.

Clinical information relating to streptococcal-induced interstitial nephritis is sparse. Kannerstein made brief mention of proteinuria, white cells and casts as a common finding, although urinalysis was available in less than one-half of his cases. He gave no data relating to renal function. Neither Mallory and Keefer nor Brody and Smith reported clinical data beyond blood cultures. Lyttle[1] carried out thrice-weekly Addis counts on 14 boys, ages 4-14, hospitalized with scarlet fever. Every patient showed Addis-count abnormalities, beginning most often during the first week of illness and lasting as long as 45 days. In addition to increased protein and cellular components, an increased number of casts was observed, but further characterization of the casts was not done. None of the patients died, none developed complications, and all recovered satisfactorily. No histologic studies were done, therefore, to correlate with urinalysis, not only because of the mildness of the illness, but also because the technique of percutaneous biopsy was not yet available. Lyttle did not include information relating to renal function or blood pressure, but he did review the clinical literature dealing with urinary changes during scarlet fever. Most previous authors, using widely varying screening methods, had found abnormalities in the urinalysis in approximately 50% of their patients, and nearly all subjects were children in every study. In one review of 180 cases of scarlet fever presented by Thompson,[10] 112 cases had albuminuria or hematuria, or both, "with or without edema." Two additional patients showed anasarca in the absence of urine abnormalities. Since no histologic data are available, it cannot be determined which of these patients might also have suffered from acute glomerulonephritis.

The most complete picture of severe streptococcal-induced AIN was presented by Knepshield[4] in 1969. A three-year-old girl developed anuria and anasarca 12 days after the onset of acute streptococcal infection characterized by fever, erythematous,

blotchy rash, and suppurative submandibular adenitis from which Group A, Beta-hemolytic streptococcus was isolated. Treatment with penicillin and sulfonamide was begun on the 13th day of illness and later penicillin alone was used. On day 14, urinalysis showed 5-10 red cells, 5-10 white cells, numerous renal tubular cells, and a moderate number of granular, waxy and hyaline casts. Severe oliguria persisted for a total of 9 days, and peritoneal dialysis was carried out. No eosinophilia was present. Renal biopsy was performed which confirmed the diagnosis of acute diffuse interstitial nephritis. The child made a satisfactory recovery on penicillin therapy. Another recent case of suspected AIN in a 5-year-old boy with a severe Group A Beta-hemolytic streptococcal infection was reported by Haddow, et al.[5] Biopsy was not performed, but acute renal failure began during the first 24 hours of infection and subsided over the next 4 days, while the infection was under treatment with penicillin. Dialysis was not required, and abnormalities of urinalysis were similar to those already mentioned. Recovery was complete.

The renal lesion as defined by light microscopy is characterized by infiltration predominantly with mononuclear cells, a few polys and eosinophils also being present. Brody and Smith[7] describe the infiltrate as beginning in the adventitia of long veins on the boundary zone between medulla and cortex. The infiltrate then appears in the interstitium around the small veins and gradually spreads throughout the interstitium, rarely being seen within the tubules. Glomeruli may be completely surrounded, but invasion does not occur. Knepshield's case report[4] provides the only recent pathological data. He describes a diffuse interstitial infiltrate of lymphocytes, plasma cells, and eosinophils with a moderate degree of interstitial edema. Proximal tubules show dilated lumina, swelling of individual lining cells, and frank necrosis. This pathologic study includes also the only available electron microscopic study, including the tubular pathology. Glomeruli are normal by both light and electron microscopy.

While we have focused attention on the kidney as a target organ for acute streptococcal insult, it must be stressed that other organs are also subject to insult, during the course of such infections. Many of the pathological studies already quoted[7,9] give extensive descriptions of mononuclear cell infiltrates in heart and liver, as well as similar lesions in adrenals and spleen, and most recent clinical reports include hepatitis,[11,12] abnormalities in liver chemistries,[5] and Coombs positive hemolytic anemia.[4]

Acute Interstitial Nephritis Associated With Antibiotics

The association between AIN and antibiotics has been recognized for over thirty years. Nearly 50 cases have been reported with varying degrees of documentation.[3,13-28] In adults a clinical or pathological picture of AIN has been associated with penicillin,[19] methicillin,[18,20] oxacillin,[21] ampicillin,[22] sulfonamides,[23,24,27] P-Amino salysilic acid,[25] nitrofuradantin,[28] and a number of other drugs and toxins.[3,25,29] In children a total of 9 cases of antibiotic-associated nephropathy have been reported, all being associated with complete recovery. Grattan[13] reported a 5½-year-old child with cystic fibrosis who exhibited a recurrent clinical picture of AIN with each of multiple 3 to 6 day exposures to methicillin. No biopsy was performed. Renal pathology at autopsy 6 months after the last episode was normal. Carre[14] reported 3 cases in children, two of whom apparently suffered an accelerated hypersensitivity reaction after receiving penicillin and developed anuria within 24 hours. The third child developed anuria after 5 doses of oral sulfonamide. No biopsies were done. Zilbey[15] reported one case of anuria occurring 34 hours after an intramuscular penicillin injection in a 1½-year-old girl. Feigin and Fiascone[15] reported a 2½-year-old girl who, after a 2-week oral course of penicillin and sulfonamide for otitis media, developed a pulmonary abscess. She was treated with intravenous methicillin, and nephritis developed. No biopsy was performed. Brauninger and Remington[18] reported 2 children treated with high doses of intravenous methicillin who developed a clinical picture of AIN 2 and 3 weeks respectively into treatment. No biopsy information is available. Tannenberg, et al[17] reported a 12-year-old treated with ampicillin for a carbuncle which grew staphylococcus, who rapidly developed the clinical laboratory picture of AIN. The renal biopsy done at 3 weeks represents the only pathologically documented pediatric case of antibiotic-induced AIN in the literature. As a result, the bulk of available histologic information is derived from adult studies.

A minimum of one day, but more often one to four weeks, of therapy is required before AIN appears. The route of drug administration does not appear important. Early urinary manifestations are hematuria and proteinuria, followed by pyuria, cylindriuria and renal tubular cells. Red cell casts are absent in all pathologically documented cases. Evidence of renal tubular dysfunction such as decreased concentrating and acidifying ability may also occur.[26] Urine output may remain normal or progress rapidly to anuria and acute renal failure. Serum urea nitrogen and creatinine correspond with the degree of renal failure. Eosinophilia of up to 40% may be present and be recognized before renal dysfunction manifests itself. In some cases, both the degree of eosinophilia and the height of serum IgG levels have correlated with increasing disease severity.[22] IgE levels have been reported recently in 5 cases of acute interstitial nephritis, with elevations in 3 and with changes correlating with clinical status in 1.[38]

Patients may exhibit fever, lethargy, a morbilliform, erythematous or urticarial rash, abdominal pain, and occasionally, flank pain. Bacterial cul-

tures prior to instrumentation have usually been negative, thus excluding bacterial pyelonephritis. There are no reports of viral isolation or serologic investigation, nor have attempts been made at an anaerobic bacterial isolation.

The course of AIN varies from prompt resolution after drug discontinuance to prolonged renal failure. Even with severe AIN, most patients recover completely, but some adults have shown evidence of persistent low grade renal dysfunction or mild hypertension.[20] Acute recurrence of AIN has occurred with inadvertent re-exposure to the original drug or a homolog.[12,22] Treatment has been aimed at managing renal failure, discontinuing the suspected agent, and, in some cases, giving steroids based on the clinical impression that they may be of benefit.[19,22,23] Unger and Nemuth[40] treated one patient with penicillin-induced nephritis with penicillinase, achieving prompt clinical resolution. This treatment has not been tried again, and its merits cannot be accurately assessed.

The pathology of antibiotic-associated AIN is well described in adults.[3,19,20,22,26] There is only one such report in a child.[17] Kidneys may be grossly normal, or may appear edematous and pale with patchy cyanosis and loss of the cortico-medullary border on cut section. There is, ordinarily, normal glomerular cellularity with at most minimal capillary dilatation or thickening. An intense generalized interstitial cell infiltrate is present, consisting predominantly of lymphocytes, but with a significant number of plasma cells and eosinophils. Polymorphonuclear leukocytes may be noted adjacent to necrotic areas and in a perivenous distribution. In one case of sulfonamide-associated AIN biopsied early, polymorphonuclear cells predominated: a follow-up biopsy three months later demonstrated predominantly round-cell infiltration.[23] Mild to severe interstitial edema is common. Tubules show focal areas of mild to severe damage, with amorphous fibrillar casts, cellular necrosis and regeneration.[22,26] Electron microscopic studies have confirmed light microscopic results, showing a loose fibrillar electron-dense deposit in both glomerular and tubular cells adjacent to the basement membrane[22] in one study and swollen proximal tubular cells with vacuoles containing dense material in the second.[23] These areas correspond to the sites where Baldwin[26] found positive fluorescence to dimethoxphenyl-pennicilloyl haptemic groups, the major haptemic antigen of methicillin. No viral particles have been found.

Comment

The fact that accute interstitial nephritis may be produced either by the Beta-hemolytic streptococcus or by antibiotics may, at times, make definition of an etiologic agent difficult. It is possible that several cases reported as antibiotic-induced AIN may actually have been caused by streptococcal infection,[19,22,23,27] based on clinical histories of cellulitis and abnormal pre-treatment urinalyses. Since one etiology requires continuance of appropriate antibiotic therapy while the other demands discontinuance, every effort must be made to separate them. When the infectious agent is responsible, AIN is at its worst very early in treatment and subsides during therapy, while antibiotic-induced AIN appears during therapy and steadily worsens. This time sequence of AIN's appearance and course may ultimately be the most useful factor in determining etiology, although there are a number of clinical and laboratory observations which may also be of help.

Eosinophilia is frequently seen with antibiotic-induced AIN. When the streptococcus is responsible for AIN, eosinophilia appears usually when the infectious precess is subsiding, although there have also been reports of eosinophilia early in the course of scarlet fever. Skin rashes, often consistent with allergic features, have been seen as part of the antibiotic-induced AIN, while rashes other than scarlet fever are rare with streptococcal-induced AIN. IgE should be investigated in future cases to determine its possible role.

The routine urinalysis is essential for making the diagnosis of AIN. If this study is normal initially and becomes abnormal during antibiotic therapy in conjunction with other clinical signs of renal dysfunction, this would support an antibiotic etiology. If, in the presence of acute streptococcal disease, the urinalysis is abnormal prior to therapy, then streptococcal-induced AIN must be considered. In either instance, it is worthwhile to perform more extensive measurements of renal function even though biochemical changes and oliguria are uncommon. It is theoretically possible for antibiotic-induced AIN to be superimposed on streptococcal-induced AIN. Under these conditions it may not be possible to make an absolute diagnosis with present diagnostic methods.

There does appear to be some correlation between the severity or duration of acute streptococcal infection and the severity of the interstitial nephritis. It would certainly appear that many streptococci have the ability to produce infiltrates in the renal interstitium, but clinical consequences are most often mild, even in untreated cases. The usual mild urinary sediment changes occurring with acute streptococcal infections have produced varying degrees of bewilderment and concern in clinicians over the years, often being classified as "toxic" nephritis. It is reasonable to assume that such changes are, nearly always, from mild AIN and are self-limited. There is little reason for AIN to be confused with acute post-streptococcal glomerulonephritis, which appears after both infections and therapy are finished.[2,31]

Biopsies are remarkably similar under the light microscope for both streptococcal and antibiotic-induced AIN. Based on electron microscopic studies in one streptococcal[4] and two antibiotic-induced[22,23] AIN biopsies, the two processes appear

to be different. In the former, tubular basement membrane is of normal thickness, though disrupted by collagen fibers; while in the latter there are thickened tubular basement membranes. Normal tubular mitochondriae have also been found in the former, while they are decreased in the latter.[23] Further, there is no electron-dense material found when streptococcal infection has produced AIN, but when antibiotics are the cause of AIN electron-dense material has been found intracellularly in vacuoles in both cases, and in addition, subepithelially along the glomerular and tubular basement membranes in one.[22]

These data in conjunction with Baldwin's fluorescent studies and serum assays demonstrating markedly elevated IgG and IgM antibodies to penicillin in a patient with biopsy-proven AIN produced by penicillin,[26] invite the hypothesis of an antigen-antibody complex disease stimulating the inflammatory response. Serum Beta-1-C levels have been normal,[5,22] however, and the Beta-1-C and Beta-1-A components of complement have not been present in biopsy material[26] which neither confirms nor excludes an antibody complex disease. There have been no detailed studies on either the classic or alternate pathways of complement-activation,[32,33] and these investigations would appear worthwhile. Since the presence of free circulating antigen-antibody complexes or of free antibody or antigen would be further evidence in support of an immune complex disease,[34] further such studies are also indicated. A number of other animal and human studies have suggested renal tubular damage may be produced by an antigen-antibody reaction. In most of these, glomerular involvement has also been found.[34,36] Simenhoff[20] has suggested that certain drugs have a greater ability to induce AIN because they are more highly concentrated in renal tubules as part of their normal metabolism. It is not clear at present how this fact would relate to a possible antigen-antibody interaction, but it would support a direct toxic effect.

The hypothesis that streptococcal-induced AIN results from a toxin or group of toxins perhaps caused by a specific phage type as with erythrogenic toxin is partially, but not totally, supported in animal studies. Extensive investigations with individual streptococcal extracellular products, cell wall sonicates and killed organisms have provided much information concerning effects on a variety of animals.[35,38] Following injection of streptococcal extracellular products into rabbits, lesions have appeared in heart, liver, and diaphragm similar to lesions found in corresponding organs of humans dying from acute streptococcal disease. Serum enzyme changes in such animals have not been reproducible, however, with the exception of renal tubular lesions in mice after implantation of streptococci in intraperitoneal diffusion chambers, or after injections of streptolysin S.[39] This absence of renal pathology in animals might well be nothing more than a difference in species sensitivity, but it prevents final conclusions regarding streptococcal toxins as inducers of AIN. Attention has repeatedly focused on scarlet fever in association with AIN, possibly because the clinical picture is so readily identifiable. There is no evidence, however, to support the erythrogenic toxin as the sole culprit in causing AIN. It will be important in the future to correlate streptococcal typing with the presence and severity of the renal lesion to determine whether some types are more "nephrotoxic" than others.

Summary and Conclusions

The existence of acute interstitial nephritis in children is not generally appreciated in the recent pediatric literature. In the pre-antibiotic era, the most common etiology of this process was a streptococcal infection. With the advent of antibiotics, there has been a marked decrease in the recognized incidence of streptococcal-induced AIN, coupled with an increasing recognition of antibiotic-associated AIN, thus complicating the definition of an etiologic agent. The early and recent literature on the clinical, laboratory and histologic parameters of streptococcal-induced AIN have been reviewed and compared with antibiotic-associated AIN. Criteria for distinguishing the differential diagnosis have been proposed. Speculation as to the primary pathologic process in each has been put forth and appropriate therapy suggested. It is important to recognize that both entities exist so as not to diagnose mistakenly post-streptococcal acute glomerulonephritis, which has a significantly different course and well-defined prognosis. We would urge the closer scrutiny of patients with streptococcal disease so as to recognize and more accurately define the present day incidence, etiology, clinical-pathological correlates, and prognosis in each case.

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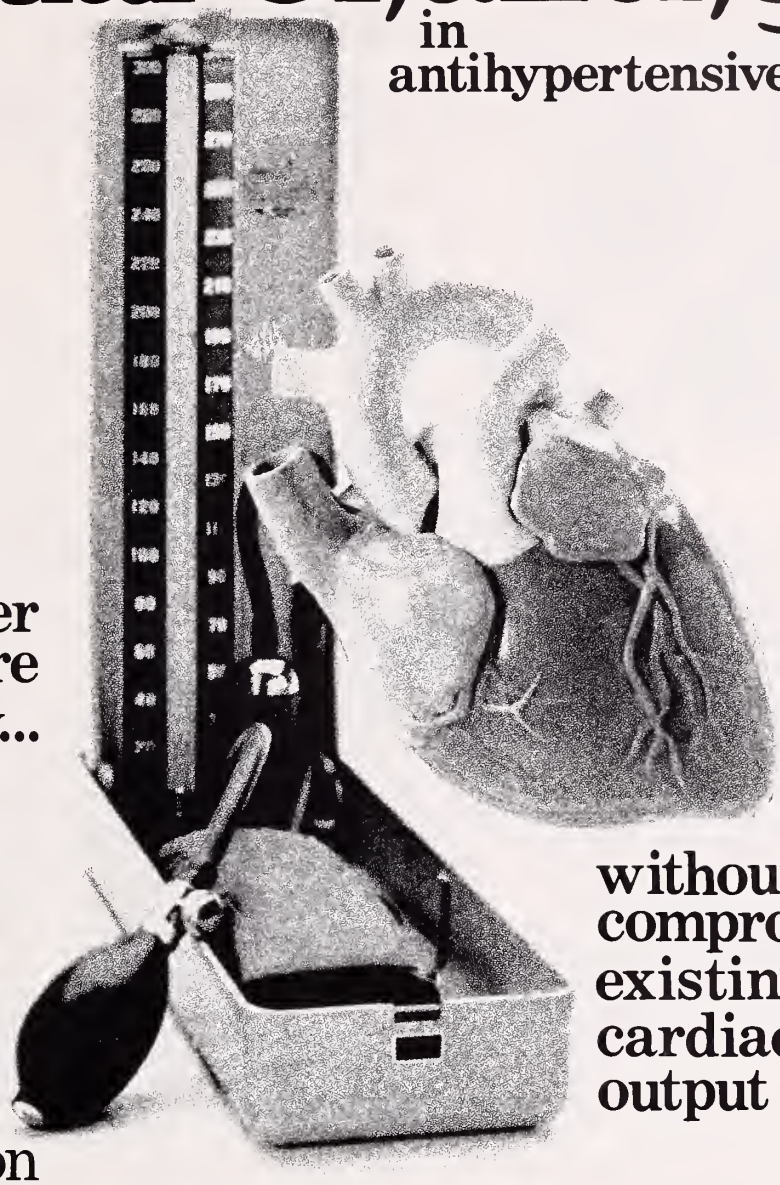

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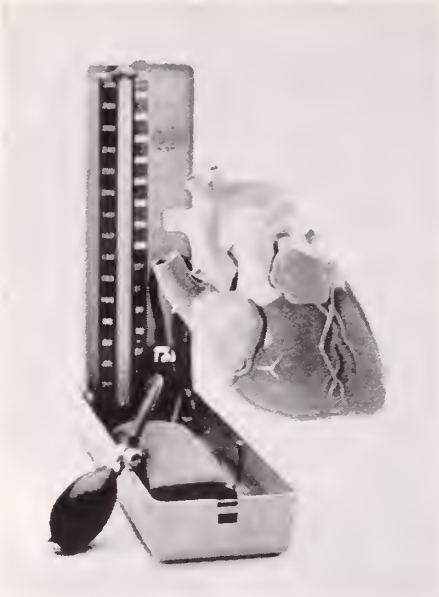

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Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, occasionally with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

Pregnancy and Nursing: Use of any drug in women who are or may become pregnant or intend to nurse requires that anticipated benefits be weighed against possible risks; possibility of fetal injury or injury to a nursing infant cannot be excluded. Methyldopa crosses the placental barrier, appears in cord blood, and appears in breast milk.

Precautions: Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of: urinary uric acid by the phosphotungstate method, serum creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: *Central nervous system:* Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, decreased mental acuity, involuntary choreoathetotic movements; psychic disturbances, including nightmares and reversible mild psychoses or depression.

Cardiovascular: Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if edema progresses or signs of heart failure appear.)

Gastrointestinal: Nausea, vomiting, distention, constipation, flatus, diarrhea, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis.

Hepatic: Abnormal liver function tests, jaundice, liver disorders.

Hematologic: Positive Coombs test, hemolytic anemia. Leukopenia, granulocytopenia, thrombocytopenia. Positive tests for antinuclear antibody, LE cells, and rheumatoid factor.

Allergic: Drug-related fever, lupus-like syndrome, myocarditis.

Other: Nasal stuffiness, rise in BUN, breast enlargement, gynecomastia, lactation, impotence, decreased libido, dermatologic reactions including eczema and lichenoid eruptions, mild arthralgia, myalgia.

Note: Initial adult dosage should be limited to 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third months of therapy; increased dosage or adding a diuretic frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

How Supplied: Tablets, containing 125 mg methyldopa each, in bottles of 100; Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 500.

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Hypoparathyroidism Resulting From Biologically Ineffective Parathormone in a Phenotypically Normal Child

JAMES E. HADDOW, M.D.,* JOEL HERSKOWITZ, M.D.,** EVA MAUER, M.D.** AND MADELINE MORRIS, M.D.**

Recent advances in the biochemical analysis of calcium homeostasis have led to more precise definition of many known disorders of calcium metabolism and to the identification of other, previously unrecognized disorders. The present case, involving a child who appears to manufacture biologically ineffective parathyroid hormone, could not have been adequately characterized without these new assays. To date, at least one similar case has been reported.[1,2] In presenting our patient, we will discuss an approach to hypocalcemic disorders of childhood as well as current diagnostic studies.

CASE REPORT

S. M., a 6-2/12-year-old black girl, presented with "sore and stiff hands" since awakening on the morning of admission to Boston City Hospital. She had lost four pounds the preceding month during which she suffered from an upper respiratory infection. She took no medicine other than aspirin and cough syrup for her recent illness in addition to 1 mg of sodium fluoride per day. For the preceding two years she had not drunk milk but had eaten one pint of ice cream per day. The two varieties of ice cream which she ingested did not contain Vitamin D.

On examination she was pleasant and cooperative. Wrists were flexed with fingers adducted and hyperextended (Figure 1). Vital signs were normal. Height and weight were in the ninetieth percentile with head circumference at the fiftieth percentile. She had an exudative tonsillitis, hypoplastic blunted teeth with brownish discoloration, and a slightly enlarged non-tender thyroid gland. Chvostek and Trousseau signs were positive. She did not have pedal spasm, unusual facies, dysplastic hands, or signs of mental retardation.

X-rays of knees, hand, chest, and teeth all were normal, as was electrocardiogram. Laboratory studies were as follows: complete blood counts, erythrocyte sedimentation rate, sickle cell screening test, Mantoux test and throat culture all were normal. Blood urea nitrogen was 3mg/100ml, creatinine 0.9mg/100ml, serum sodium 146m Eq/1. Arterial pH was 7.47 with pCO_2 29. Total thyroxin was 11.7 micrograms/100ml. A stool sample was negative when stained for fat.

Serum calcium measured on eight occasions showed a mean value of 6.6mg/100ml (range 6.2 - 6.8), serum phosphorus showed a mean value of 5.5mg/100ml (range 4.7 - 5.8). Serum magnesium was 2.0 and 2.3mEq/1 on two occasions. Serum immunoreactive parathyroid hormone (IPTH) was 168 microlitre Equivalents/ml (upper limit of normal is 90). Serum alkaline phosphatase was 10.8 Bodansky Units (B.U.) (adult normal is 0.8 - 2.3). Serum 25 hydroxy cholecalciferol (25 OHD_3) was unmeasureably low. Urine analyzed quantitatively for amino acids contained 4.9mg/100ml cystine, 1.8mg/100ml ornithine, and 16.3mg/100ml lysine, all elevated. Other amino acids were normal.

On the fourth hospital day, parathyroid hormone was administered intravenously and urine collected for cyclic AMP, phosphorus and creatinine. Figure 2 depicts the results of that study. The baseline cyclic AMP value was low in relation to the high serum IPTH level. PTH infusion resulted in a normal cyclic AMP response and urinary phosphorus also rose appropriately.

The patient was begun on dihydrotachysterol (Philips Roxane) 0.6mg daily. The dose was lowered to 0.2mg daily as serum calcium normalized and treatment was later changed to Vitamin D, 400 I.U. daily. Serum calcium became normal within two weeks of beginning therapy during which time the phosphorus rose to 6.5mg/100ml. Five post-treatment serum calcium determinations over a three month span showed a mean of 9.9mg/100ml (range 9.3 - 10.8) with phosphorus 6.2mg/100ml (range 5.2 - 7.2). Alkaline phosphatase was 9.45 and 7.0 B.U. on two occasions. Serum IPTH was in the low normal range on two occasions after normalization of serum calcium. Urine amino acid pattern remained abnormal.

Two sisters, mother, maternal uncle, maternal grandfather, and maternal grandmother were tested for serum calcium, phosphorus, and alkaline phosphatase. None had findings similar to those of the patient.

DISCUSSION

When faced with the problem of hypocalcemia in a child, one should consider the three groups of disorders described in an earlier publication [3] under the headings of a) *Disorders Associated with Rickets*, b) *Hypoparathyroidism*, and c) *Pseudohypoparathyroidism*. The differential diagnostic possibilities can ordinarily be narrowed considerably as soon as history, physical examination, and x-rays are completed. The presence of rickets would, with rare exception, exclude hypoparathyroidism and pseudohypoparathyroidism immediately; then the possible rickets-producing diseases could be further investigated.[4-7] With the exception of renal failure, all rachitic diseases are associated with low serum phosphorus due to the effect of elevated endogenous PTH on the kidney. Forms of rickets which are not associated with hypocalcemia (example: familial hypophosphatemic rickets),[8] are purposely omitted from this discussion.

The hypocalcemic child without rickets would fall into the category of hypoparathyroidism or pseudohypoparathyroidism. Both categories would have a normal to high serum phosphorus value in the face of hypocalcemia. Certain syndromes such as the classical form of pseudohypoparathyroidism,[9] hypoparathyroidism with moniliasis and Addison's disease,[10] and congenital absence of thymus and

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Fig. 1. Photograph of the patient's hand shortly after admission.

parathyroids[11] would be readily identifiable. A hypocalcemic child without rickets but with normal phenotype could have some other form of either hypoparathyroidism or pseudohypoparathyroidism, and further laboratory studies would be required for accurate definition.

The present patient was not rachitic, had a normal phenotype, and had a high normal serum phosphorus level[12] in the face of hypocalcemia. She thus represented some form either of hypoparathyroidism or pseudohypoparathyroidism. The absence of stigmata on physical examination further excluded several diagnoses listed under all three headings, and diagnostic studies were undertaken to characterize her condition more precisely.

Recently, it has been possible to measure serum immunoreactive parathyroid hormone.[13,14] The test, while difficult to standardize and perform, has proven important in understanding disorders of calcium metabolism. Different molecular species of IPTH have been identified, some more biologically active than others,[2,15-17] through techniques for such differentiation are not yet clinically available. When evaluating serum IPTH levels one must consider the level of serum calcium, since IPTH should be very low in the face of hypercalcemia and vice versa. Our patient had a very elevated level of IPTH, an appropriate response to hypocalcemia. Her high-normal serum phosphorus, however, suggested an abnormal renal response to endogenous parathyroid hormone.

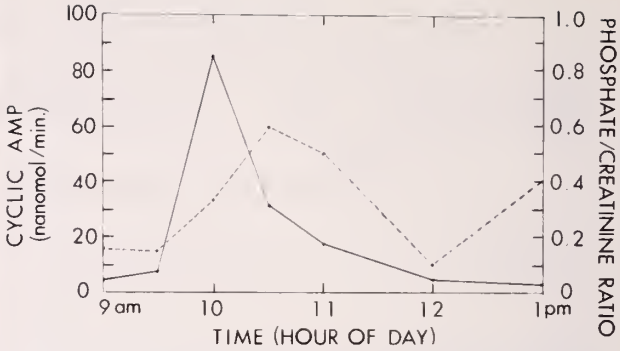

Fig. 2. Cyclic AMP (solid line) and phosphate (dotted line) excretions in urine following intravenous infusion of 300 units parathyroid hormone (Lilly) between 9 and 9:30 A.M.

Renal response can be studied by infusing exogenous parathyroid hormone of known potency, according to the procedure of Chase, et al.[18] Intravenously infused parathyroid hormone normally provokes a large outpouring of cyclic AMP in the urine, presumably as it signals the renal tubular cells to release "second messenger." Our patient responded to the infusion with a normal twenty-fold rise in urinary cyclic AMP and an appropriate increase in urinary phosphate. In view of this normal response and from the fact that her baseline cyclic AMP values were low in relation to her circulating IPTH, we conclude that renal tubular response to exogenous PTH was intact and that her own parathyroid hormone was not biologically effective.

It has recently been possible to measure serum 25 OH D_3.[19] While this is not the final form of Vitamin D, it is a good indicator of Vitamin D sufficiency. Our patient's low serum level indicated an insufficient Vitamin D intake which we suspect to have been superimposed upon her underlying problem, producing tetany and prompting her to seek medical attention.

Serum magnesium levels were normal in our patient, and there was no indication that she was magnesium deficient. Magnesium deficiency may be responsible for a variety of alterations in calcium homeostasis, including both suppression of PTH release and end organ unresponsiveness to PTH.[20-23] When magnesium deficiency occurs, either with poor dietary intake as in chronic alcoholism or as a result of magnesium malabsorption, the affected individual can present with hypocalcemia and hyperphosphatemia. Under such conditions, magnesium replacement would correct the problem.

Urinary amino acid levels were measured as part of this patient's evaluation. Secondary hyperparathyroidism is ordinarily associated with a generalized aminoaciduria.[6] The reason is obscure, although presumably parathormone alters renal tubular function. The aminoaciduria disappears as secondary hyperparathyroidism resolves. Our patient had elevated levels of cystine, ornithine and

lysine initially, with other urinary amino acids being normal. These abnormalities persisted after serum IPTH and serum calcium levels returned to normal. The urinary amino acid pattern may represent part of this patient's disorder of calcium metabolism or may represent the recessive pattern of cystinuria.

Our patient responded to Vitamin D therapy with a rise in serum calcium and a fall in serum IPTH. The serum phosphorus became further elevated, at times being clearly abnormal. This may indicate that the patient's own IPTH had some renal tubular effect in high concentrations or that gut phosphate absorption was diminished as part of the Vitamin D deficiency state.

At present the classification of pseudohypoparathyroidism is undergoing rapid change. Until recently only the classical form described by Albright was known: end-organ unresponsiveness to PTH combined with short stature, obesity, mental retardation, and short metacarpals.[18,24-29] Since then, several conditions have been described, usually in association with a normal phenotype in which either the end-organ or PTH itself is defective.[1,30-32]

Beginning in 1962, reports have appeared describing pseudohypoparathyroidism with normal phenotype and osteitis fibrosis cystica. More recently such patients have been shown to have elevated levels of IPTH and poor or absent renal response to exogenous parathyroid hormone. The fact that these individuals suffer from osteitis fibrosis cystica suggests that the bone is normally responsive to circulating PTH. A few of these patients also have had metaphyseal lesions mimicking rickets.[32] These cases of pseudohypoparathyroidism with rachitic changes do not fit well into the classification of hypocalcemia proposed here.

Hypomagnesemia has produced reversible end-organ unresponsiveness to PTH in a group of alcoholic patients studied by Estep.[20] Under other clinical circumstances, hypomagnesemia has suppressed PTH production while end-organ responsiveness remained normal.[21,22] Thus, while reports of magnesium's role in hypocalcemia are conflicting, it must be considered as a possible etiologic agent for pseudohypoparathyroidism.

In 1973, Nusynowitz and Klein[1] described the first case of ineffective endogenous PTH in a 20-year-old male with hypocalcemia, hyperphosphatemia, chronic tetany and cataracts. Phenotype was normal. Bones appeared undermineralized but rickets and osteomalacia were absent. Serum IPTH was elevated in one laboratory but normal in another, suggesting that different forms of IPTH were being assayed. Renal responsiveness to exogenous PTH was normal as indicated by measurements of urinary cyclic AMP and phosphorus. They postulated a precursor hormone which could not be converted to active PTH due to an enzymatic defect.

Our patient likewise seems to demonstrate production of ineffective PTH assayed, so far, in only one laboratory. Her PTH is markedly elevated in the face of hypoparathyroid-like clinical and laboratory findings, suggesting poor biologic activity. The normal renal response to exogenous PTH further supports this conclusion. Without osteitis fibrosis cystica, the patient appears to lack biologic activity of her PTH in bone as well as in kidney.

Summary

The present patient, a 6-year-old black female of normal appearance and intelligence, developed hypocalcemic tetany during an acute respiratory infection. Serum magnesium was normal, serum phosphorus was high normal, and immunoreactive parathormone was elevated. She had been on a Vitamin D deficient diet for the preceding two years, and serum 25 OH D_3 levels were low. There was no radiographic evidence either of rickets or of osteitis fibrosis cystica. Intravenous infusion of parathormone induced a normal rise in urinary cyclic AMP and phosphorus. Treatment with dihydrotachysterol produced normalization of serum calcium and IPTH, but serum phosphorus rose intermittently above the normal range. Urinary amino acids showed selective increase of cystine, ornithine, and lysine, a pattern which persisted after therapy and was consistent with the carrier state of cystinuria. The generalized increase in urinary amino acids usually associated with secondary hyperparathyroidism was not seen. Laboratory and radiologic data indicated that the patient was secreting a biologically ineffective parathormone which, with the added stress of Vitamin D deficiency and infection, produced tetany.

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Spring Meeting of the M.M.A. House of Delegates

Saturday, March 18, 1978

12:30 P.M. — Registration; 1:00 P.M. — Lunch; 2:00 P.M. — Meeting

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9:30 A.M. — Meeting of the Executive Committee

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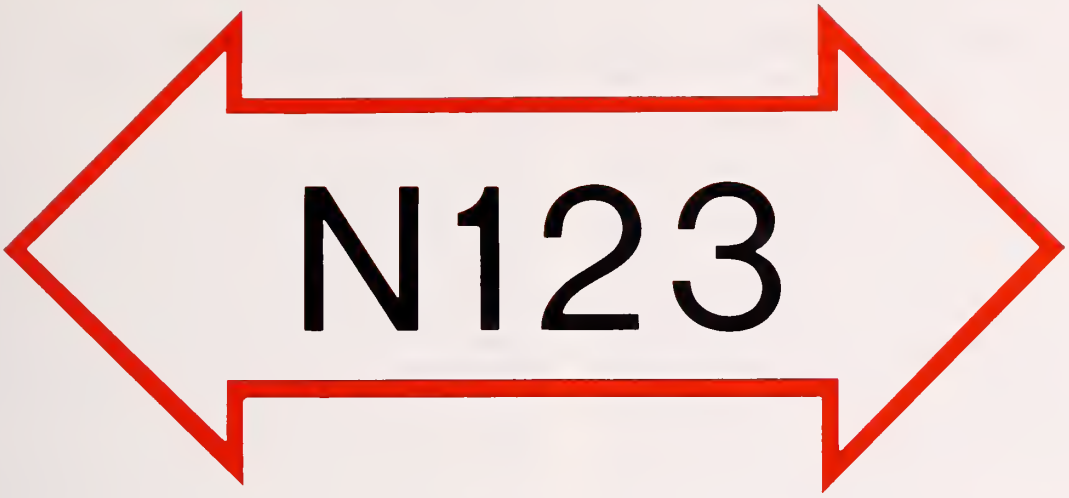

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Effects of Thorax Dimensions and Intracardiac Blood on the Vectorcardiogram†

CLIFFORD V. NELSON, Ph.D.*

A. Vectorcardiology

In this article I wish to summarize some of our findings in the field of electrocardiology and to point out their possible significance in clinical diagnosis. Our work has been mainly in vectorcardiology, in which three components proportional to left-right (X), inferior-superior (Y) and posterior-anterior (Z) cardiac electrical forces are recorded. By means of both theoretical derivations and model experiments, we have shown that it is essential to include thorax dimensions in the determination of vector magnitude.[1] We have developed a lead system based on these concepts which uses three rows of eight electrodes around the thorax for the X and Z components and a foot-head lead for the vertical or Y component.[2] The V_x and V_z voltages are multiplied by thoracic surface area and the V_y voltage by the thoracic cross-sectional area. The 24 thorax electrodes are connected to a resistor network and three output cables are connected to amplifiers to give the vector components. Potentiometers are used to adjust for individual thorax dimensions. A theoretical treatment of the method has appeared previously in this journal.[3]

Despite the increased accuracy of this system and the inclusion of thorax dimension data, it has met with limited success. One other group has used a modification of the method in which the electrodes are put on in a slightly different manner.[4] The main problem seems to have been the increased number of electrodes. The most popular lead system at present is the Frank in which only five electrodes are used around one level of the thorax.[5] At the time this system appeared, it was much better than other systems then in use, such as the equilateral tetrahedral or the cube. It was based, however, on a model of a single adult male and no provision was made for compensating for variations in shapes or sizes of patients. It would seem obvious that vector magnitudes of children, very thin or greatly obese individuals would be different from those of average normal adults. When thorax dimensions are included, the larger thorax potentials of children or thin individuals, due to closer proximity of the heart to the chest wall, are scaled down. The weight and size of the heart, of course, increase from infancy to adulthood. One would expect that the peak electrical force or "dipole moment" would increase in proportion to heart size. As the body also grows however, the distance of the heart from the thoracic walls may remain in proportion, so that the voltage may change little. By multiplying voltages by body dimensions and thereby measuring dipole moment, M, one gets a very good correlation between peak M and the heart or body weight.[6,7]

Unfortunately, there have been a number of articles written on changes in the vectorcardiogram (VCG) with age or body weight using inadequate lead systems. Not surprisingly, the results have been inconclusive. A good data base of normal values is lacking. In certain conditions, such as left ventricular hypertrophy, voltages will increase in almost any lead system. It is difficult, however, to assess the amount of hypertrophy without good standards for normal populations of various ages or weights. I have proposed a rough correction factor for common lead systems which would at least scale the results in relation to body size.[8] In this, the X and Z voltages would be multiplied by thoracic surface area and the Y voltages by cross-sectional area. The resulting figures, although not equal to dipole moment, would provide much better correlations than voltages alone. To my knowledge, this is not yet being done in any laboratory.

In recent years, many workers have been measuring the detailed distribution of potential over the thorax.[9,10] These workers have shown that the variation of potential may be complicated, particularly in patients with heart disease. In classical theory, the heart consisted of a single dipole at each instant of time with definite and continuous regions of positivity and negativity. It has been shown that there may in fact be two or more effective dipoles at certain times during QRS.[11] These extra dipoles may produce more than one simultaneous positive or negative peak of potential on the thorax. To attempt to sample such a field distribution using only five electrodes results in much information being lost.[9] Because of the inaccuracy of the simple lead systems, vectorcardiology has fallen into disrepute among cardiologists today. I believe, however, that with an adequate number of electrodes and the inclusion of thorax dimensions in the measurements, valuable information can be obtained.‡

Another example of the influence of body dimen-

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*Research Department, Maine Medical Center, Portland, Maine 04102

‡UMPG and Maine Medical Center now have a research grant from the National Institutes of Health to study ventricular hypertrophy using this lead system.

sions on the VCG is in respiration. With inspiration the voltage magnitude usually decreases. This may be due to increased distance of the heart from the chest wall, more air in the lungs or changes in heart blood volume. We have carried out some experiments in which the vector lead system was adjusted for inspiration and then for expiration on the same individual.[12] When changes in chest dimensions were compensated for, voltages increased with inspiration in some cases.

B. Effects of intracardiac blood

The electrical currents in the heart result from excitation of the myocardium. The myocardium has an electrical resistivity of about 450 ohm-cm. The blood in the cardiac cavities has a much lower resistivity, around 150 ohm-cm. The question arises as to the effects of the highly conducting blood on the myocardial currents.

In 1956, Brody showed theoretically that intracardiac blood should increase potentials due to spread of excitation from endocardium to epicardium (radial excitation) and should decrease potentials due to tangential spread along the myocardial walls.[13] We subsequently confirmed these predictions experimentally in model studies.[14,15] These effects were also studied in vivo by exchanges of packed cells or plasma for whole blood in the dog.[16] In early portions of QRS, with septal and radial free wall excitation, potentials were more than doubled by normal intracardiac blood. During late tangential excitation of the basal walls and septum, potentials were reduced by about 25 percent. The "normal" ECG is, therefore, considerably distorted by the mere presence of the intracardiac blood. During about the first half of QRS, potentials appear larger than they should be in relation to the amount of muscle mass. During the last part of QRS, potentials are smaller than they would be in a homogeneous medium. When this factor is corrected for, one should get better correlations between dipole moment and myocardial mass. These results helped to explain changes in the ECG observed in anemia and polycythemia.[17] Similar experiments in the pig indicated that excitation in the pig heart is more tangential than radial during middle portions of QRS.[18]

Studies were made of changes in the VCG after surgical correction of atrial septal defect.[19] With an atrial defect, the volume of blood in the right ventricle is greater than normal. After surgical correction, blood volumes should return to near normal. Immediate changes in the VCG should, therefore, be due to the changes in blood volumes. It was found that there were marked changes one to two weeks after surgery. In this length of time, it is doubtful that concomitant ventricular hypertrophy would regress to a significant degree.

In conclusion, the science of vectorcardiology is still in its infancy. Present standard methods are *not* "good enough for clinical purposes." It will be necessary to use more electrodes and a system tailored to the individual before meaningful and accurate results can be obtained. At present we are unable to make quantitative corrections for the effects of intracardiac blood, but these should be kept in mind.

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Epidural Venography

Maine's First 75 Examinations*

PETER E. GIUSTRA, M.D., JOHN W. WICKENDEN, M.D., ROBERT S. FURMAN, M.D., ROGER W. WICKENDEN, M.D. AND PAUL J. KILLORAN, M.D.

Selective epidural venography has established itself as a low risk, highly accurate, radiologic examination in the diagnosis of clinically suspected lumbar disc disease.[1-7] It is our purpose to present the experience at the Penobscot Bay Medical Center with Maine's first 75 examinations and to discuss our protocol for epidural venography which differs somewhat from that reported nationally.

Between January and June, 1977, 75 selective epidural venograms have been performed at the Penobscot Bay Medical Center. The examination is routinely done on an outpatient basis without premedication. Percutaneous puncture of the appropriate femoral vein is made using local anesthesia at the puncture site. Selective catheterization of an ascending lumbar vein, ipsilateral and/or contralateral presacral vein is accomplished under fluoroscopic guidance using a curved 5 French catheter.[1-7] Forty cc. of Renografin-60® is injected at a rate of 5 cc. per second using abdominal compression and Valsalva maneuver. Films are exposed at 1 per second for 12 seconds, and the film with the best venous filling is utilized for subtraction. At the termination of the procedure, manual pressure is held over the puncture site for 10 minutes; the patient is observed for 15 more minutes and returned to home with limited activity for the remainder of the day.

Contrary to what one might infer from the literature, selective epidural venography is not always a technically easy procedure. Catheterization of an ascending lumbar or presacral vein can be tedious and time consuming. Although we now complete the procedure in 30 to 40 minutes, there are instances where the examination takes twice that time. A fair amount of catheter experience is felt necessary in order to consistently obtain diagnostic epidural venograms. The variation in drainage of the epidural veins often is the primary reason for a prolonged procedure. Injection into one vein may produce filling of the veins not opacified by an earlier injection into a similar or different vein (Fig. 1.). It is necessary, then, to be aware of the variation of venous drainage in order to obtain complete venograms and obviate errors in interpretation secondary to incomplete venous filling. The reader is referred to previous manuscripts for more detailed description of technique, normal anatomy and basic interpretation.[1-7] In our experience, once there is sufficient filling of the epidural veins, interpretation is generally not difficult although we have found it necessary to send a few cases out for interpretive consultation. Gargano insists that multiple injections be employed routinely in order to avoid errors of interpretation.[2] Gershater states that if filling is complete in 1 injection, the examination may be terminated.[4] We agree with Gershater but have found it necessary to use more than 1 injection in over 50% of the patients. Our usual approach is to inject a left ascending lumbar vein via a left femoral vein puncture and, if necessary, a right presacral vein from the same puncture site.

In patients who have had both epidural venograms and myelograms, most would prefer to have an epidural venogram. Although there have been no complications in our first 75 patients, the examination can be somewhat uncomfortable. Even though the appropriate groin is felt to be well anesthetized with local anesthesia, the patients often feel an uneasy pressure sensation with percutaneous puncture of the femoral vein. As one cannot palpate the femoral vein, it is necessary to puncture a site medial to the palpable femoral artery. Occasionally, the femoral vein may be either on top of or underneath the artery and several attempts will be necessary in order to puncture the vein. During the contrast injection, the abdominal compression used can be uncomfortable. When the epidural venous plexus is well filled, backache is a common sequela lasting up to 30 seconds. The backache does not seem intolerable for the patient, however, and is decidedly less uncomfortable than an abdominal aortogram, for example. Soreness and ecchymosis at the puncture site for several days following the examination may occur, but such sequelae are rare and we have had no problems with bleeding or hematomas. Epidural venography completely avoids the potential of arachnoiditis or postspinal headache asssociate with myelography.

Epidural venography has been used almost exclusively in patients with negative or equivocal myelograms and clinical evidence of lumbar disc disease.[1-7] Even in those patients with positive epidural venograms, confirmatory myelograms are usually performed. Our protocol differs in that we utilize epidural venography as the initial and usually the sole invasive diagnostic radiologic procedure in the evaluation of these patients (Figs. 2-3). Myelography is used only in patients with nondiagnostic venograms or in patients suspected of spinal stenosis or tumors. Therefore, the number of myelograms performed at our institution has de-

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Fig. 1A

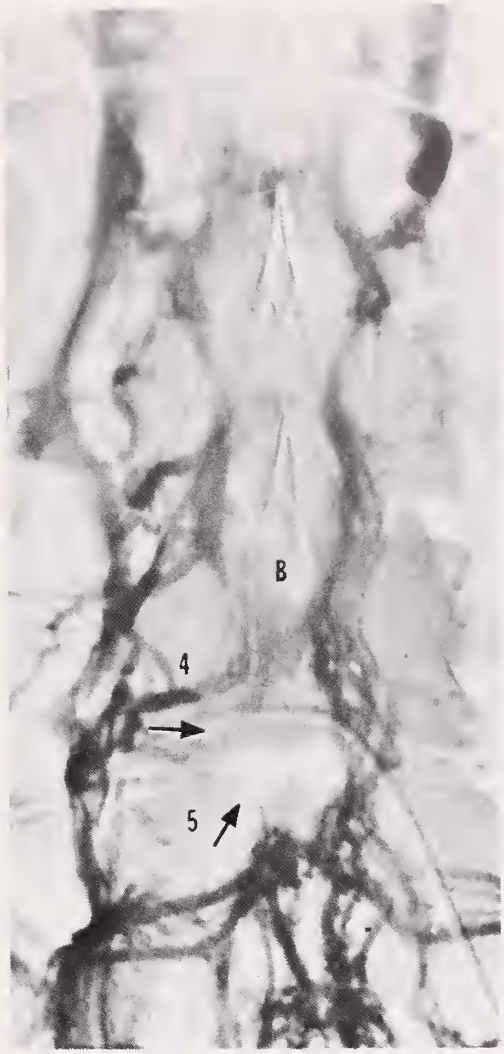

Fig. 1B

Fig. 1. A) Injection into a left ascending lumbar vein (arrow) produces excellent filling of the epidural plexus above the level of L4. Veins below L4 are not adequately opacified.

B) Injection into a right presacral vein produces excellent filling of all the lumbosacral epidural veins, especially those below L4. Surgery confirmed a ruptured intervertebral disc at L4-5 on the right where the anterior internal vertebral veins are occluded (arrows).

creased considerably since the availability of epidural venography. Because there have been no complications and the examination can be performed on an outpatient basis, epidural venography probably is performed more frequently than would be the case if only myelography were available. In the past, myelography was reserved for patients scheduled for lumbar disc surgery. Epidural venography lends itself to the evaluation of patients with acute lumbar disc symptoms even if they are not initially felt to be surgical candidates in order to more accurately establish the diagnosis of herniated disc disease and therefore more knowledgeably manage the patient. Table 1 shows that our accuracy with epidural venography in surgically confirmed cases has been noteworthy. There have been no false-positive interpretations. In only three of the twenty-five surgically confirmed positive cases has myelography been performed. Of those patients who have not undergone surgery, eight had positive venograms, thirty-three had negative, and five had equivocal studies.

Table 1

Diagnostic Accuracy of Epidural Venography (29 surgically confirmed cases)

Venography		*Surgical Findings*	
Positive	25	Positive	26*
Equivocal	2	Equivocal	2
Negative	2	Equivocal	2

*One patient had disc disease surgically confirmed at L4-5 and L5-S1. The epidural venogram was positive at both levels but initially reported to be abnormal only at L5-S1.

Besides the patients with acute lumbar disc symptoms, patients with chronic diagnostic back problems, compensation related injuries, spondylolis-

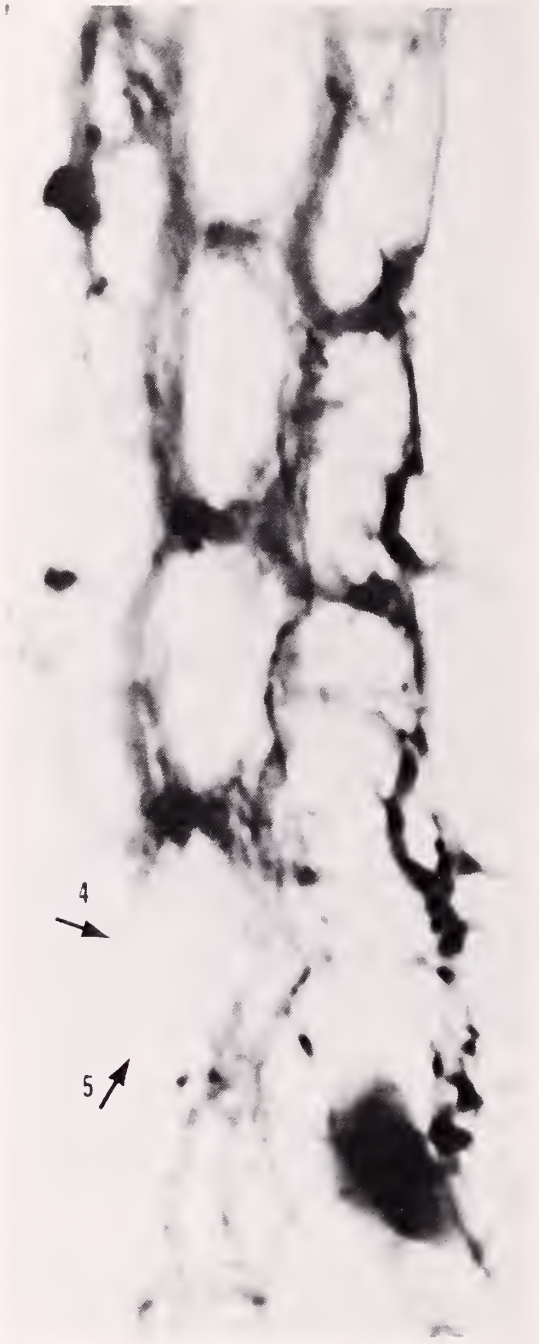

Fig. 2

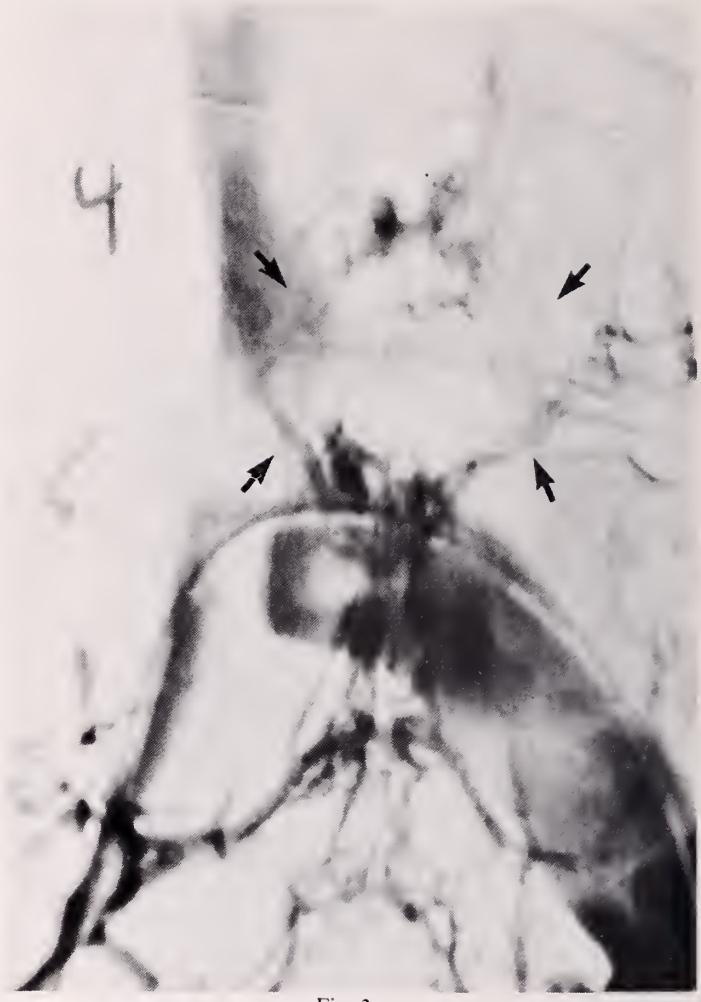

Fig. 3

Fig. 2. Injection into a left ascending lumbar vein demonstrates complete occlusion of the right anterior internal vertebral veins at L4-5. Surgery confirmed a herniated disc with a large free fragment.

Fig. 3. Injection into a right presacral vein via a left femoral vein puncture demonstrates compression and marked lateral deviation of the anterior internal vertebral veins at L4-5 bilaterally. There is some reflux into the iliac veins and inferior vena cave. Surgery confirmed a larger centrally herniated disc.

thesis, or arachnoiditis from previous myelograms or surgery, and postoperative disc patients all lend themselves to investigation by epidural venography. Contrary to other authors,[1,2] we have found the epidural venogram to be particularly helpful in patients scheduled for back fusion for symptomatic spondylolisthesis, decompression laminectomy and fusion for degenerative hypertrophic spondylosis and in patients who have had previous disc surgery presenting with recurrent disc symptoms (Fig. 4.). Although an abnormal epidural venous pattern has been reported at the levels of spondylolisthesis or previous disc excision, in our experience a normal venogram may be obtained excluding intercurrent or recurrent disc herniation (Fig. 5.). In the case of a scheduled fusion, a negative epidural venogram would obviate the need for laminectomy in conjunction with the fusion. Of the seven patients who have had surgically confirmed recurrent disc disease or spinal stenosis from hypertrophic degenerative change either at the site of previous surgery or at another disc level, all have had positive epidural venograms.

Epidural venography should become a routine diagnostic procedure at institutions in Maine in

Fig. 4

Fig. 4. Injection into a right presacral vein via a left femoral vein puncture demonstrates compression and partial occlusion of the left anterior internal vertebral veins at L5-S1. A large recurrent disc fragment was surgically confirmed.

Fig. 5. Injection into a right presacral vein (arrow) via a left femoral vein puncture produces excellent bilateral filling of all epidural veins from the sacrum through L1. Normal examination in a patient with spondylolisthesis.

Fig. 5

radiology departments with present catheterization capabilities. As Table 1 indicates, surgical correlation with positive epidural venograms is excellent. Although there is a reported false-negative rate of approximately 10%, at our institution patients with negative epidural venograms rarely come to surgery.

Acknowledgement

The authors are indebted to Fredie P. Gargano, M.D., Miami, Florida, and Raziel Gershater, M.B., Ontario, Canada, for their invaluable consultative and interpretive assistance.

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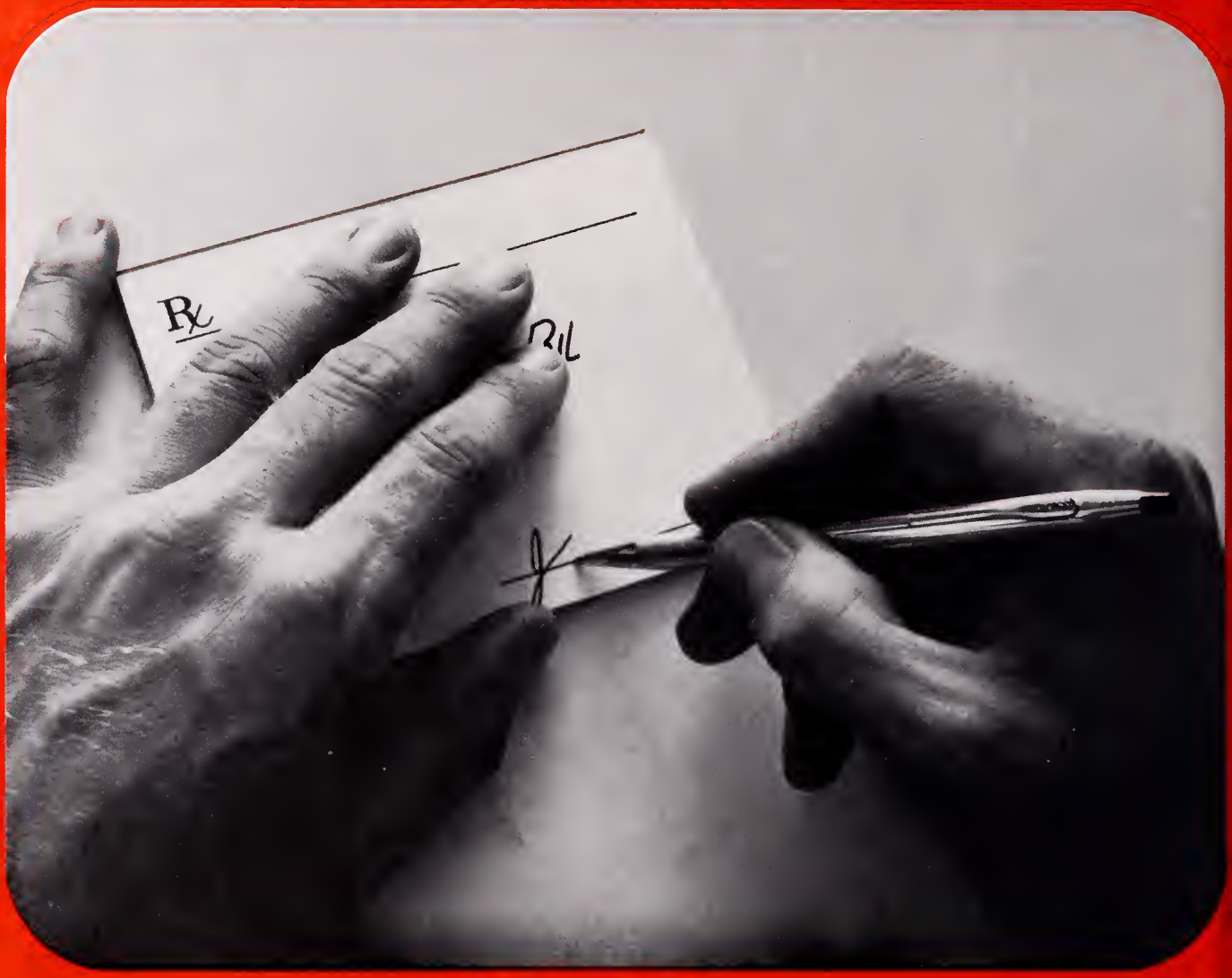
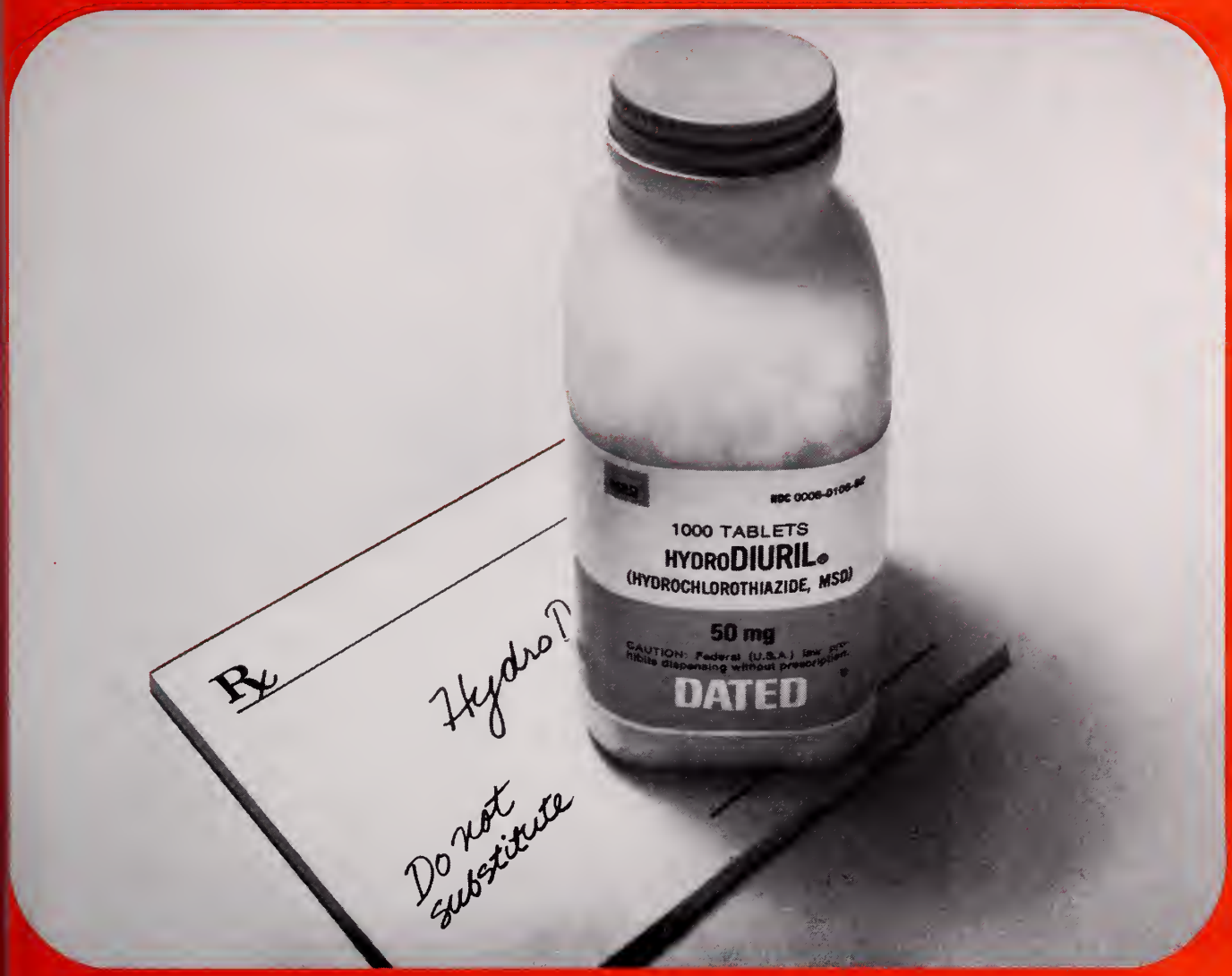
There is no substitute



yours...

Contraindications: Anuria; hypersensitivity to this or other sulfonamide-derived drugs.
Warnings: Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects may develop in patients with impaired renal function. Use with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma. May add to or potentiate action of other antihypertensive drugs; potentiation occurs with ganglionic or peripheral adrenergic blocking drugs. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possibility of exacerbation or activation of systemic lupus erythematosus has been reported. Lithium generally should not be given with diuretics because they reduce its renal clearance and add a high risk of lithium toxicity. Read circulars for lithium preparations before use of such concomitant therapy. *Use in Pregnancy:* Thiazides cross placental barrier and appear in cord blood; in pregnancy, weigh anticipated benefit against possible hazards to fetus, including fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions that have occurred in adults. *Nursing Mothers:* Thiazides appear in breast milk; if use of drug is deemed essential, patient should stop nursing.
Precautions: Perform periodic determination of serum electrolytes to detect possible electrolyte imbalance. Observe all patients for clinical signs of fluid or electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting. Hypokalemia may develop, especially with brisk diuresis, in severe cirrhosis, with concomitant corticosteroid or ACTH therapy, or with inadequate oral electrolyte intake. Hypokalemia can sensitize or exaggerate response of heart to toxic effects of digitalis (e.g., increased ventricular irritability). Hypokalemia may be avoided or treated by use of potassium supplements, such as foods with a high potassium content. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt except in rare instances when the hyponatremia is life threatening. In actual salt depletion, appropriate replacement is the therapy of choice.
Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged; latent diabetes mellitus may become manifest. Thiazides may increase responsiveness to tubocurarine. Antihypertensive effects of the drug may be enhanced in post-sympathectomy patients. May decrease arterial responsiveness to norepinephrine; this diminution is not sufficient to preclude effectiveness of the pressor agent for therapeutic use. If progressive renal im-

for experience—



or ours.

pairment becomes evident, consider withholding or discontinuing diuretic therapy. Thiazides may decrease serum PBI levels without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. Pathologic changes in the parathyroid gland with hypercalcemia and hypophosphatemia have been observed in a few patients on prolonged therapy; thiazides should be discontinued before testing for parathyroid function.

Adverse Reactions: *Gastrointestinal System*—Anorexia; gastric irritation; nausea; vomiting; cramping; diarrhea; constipation; jaundice (intrahepatic cholestatic jaundice); pancreatitis; sialadenitis.
Central Nervous System—Dizziness; vertigo; paresthesias; headache; xanthopsia.
Hematologic—Leukopenia; agranulocytosis; thrombocytopenia; aplastic anemia.
Cardiovascular—Orthostatic hypotension (may be aggravated by alcohol, barbiturates, or narcotics).
Hypersensitivity—Purpura; photosensitivity; rash; urticaria; necrotizing angiitis (vasculitis) (cutaneous vasculitis); fever; respiratory distress including pneumonitis; anaphylactic reactions.
Other—Hyperglycemia; glycosuria; hyperuricemia; muscle spasm; weakness; restlessness; transient blurred vision.
Whenever adverse reactions are moderate or severe, thiazide dosage should be reduced or therapy withdrawn.

Note: When used with other antihypertensive drugs, careful observations for changes in blood pressure must be made, especially during initial therapy. Dosage of other antihypertensive agents must be reduced by at least 50 percent as soon as this drug is added to the regimen. As blood pressure falls under the potentiating effect of this agent, further reduction in dosage, or even discontinuation, of other antihypertensive drugs may be necessary.

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Immunological Characterization of the Human Breast Cyst Progesterone Binding Protein (CPP) — A Marker for Breast Cancer?*

D. DUFOUR**, M. PAGE, L. GAUVIN, AND P. M. GAGNON***

INTRODUCTION

There is to date no correspondence between the high incidence of the human breast cyst disease and the constituents found in this pathological fluid. The major reports are works of Pearlman, who made a biochemical study of a specific progesterone binding protein in cyst fluid[1] and of Haagensen, who made an immunological study of cyst fluid proteins and described a protein which is immuno-chemically identical with a normal human milk constituent.[2]

Based on these premises, we carried out the present study on the purified specific progesterone protein binding (CPP) to determine if this constituent is *identical* to Haagensen's already described protein and to ascertain if the CPP could be a marker for breast cancer.

*Supported by the Medical Research Council of Canada.
**Laboratoire Expérimental de Biomédecine et Centre de Recherche de l'Hôtel-Dieu de Québec, Université Laval.
***Centre Hospitalier Universitaire, Laval, Québec.

MATERIALS AND METHODS

The CPP was *isolated* by the method described by Pearlman with the aid of the DEAE cellulose

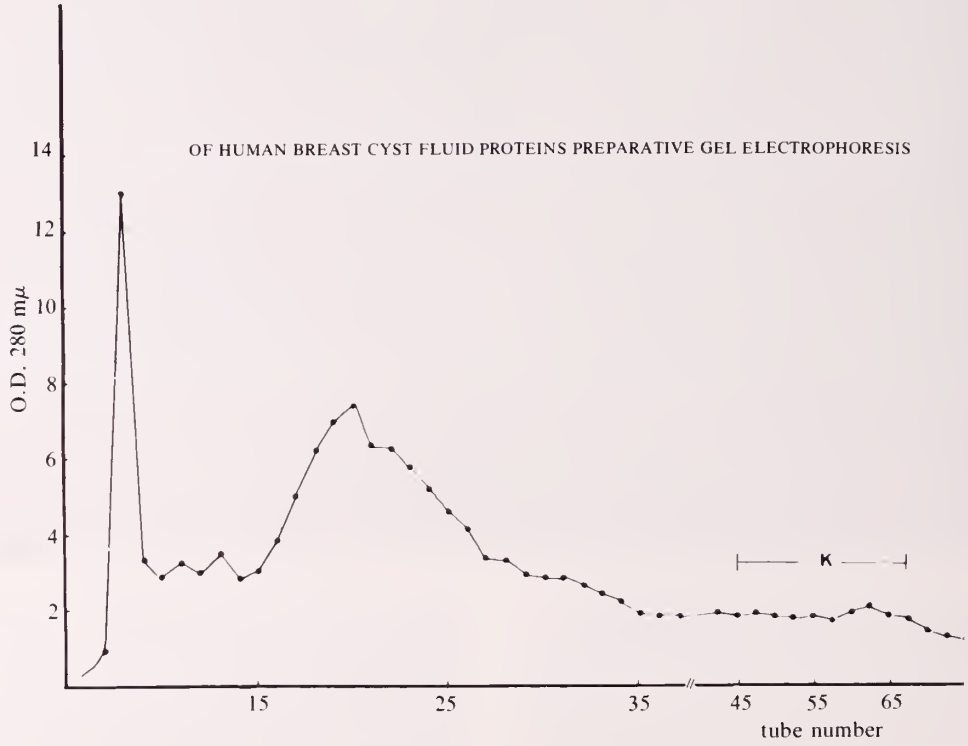

Fig. 1. Elution Profile of human breast cyst fluid proteins obtained by preparative polyacrylamide gel electrophoresis.

Technical data: The sample (4 ml of fluid containing 120 mgs of proteins) was dialysed overnight against the elution buffer (40 mM Tris-HCL pH 8.9) and was introduced in a column (2.5 cm x 10 cm) containing a 7% polyacrylamide gel. Electrodes buffer: 20 mM Tris-Gly pH 8.3. Elution buffer rate was 20 ml/h. Electrophoretic conditions 15 W., during 15 hours.

Each fraction was evaluated for qualitiative content by analytical gel electrophoresis and by immunoelectrophoretic analysis against anti normal human serum proteins antibody and against anti-breast cyst fluid proteins antibody. Fraction *K* was judged to contain a semi purified human cyst fluid protein, as illustrated in Figures 2 and 3.

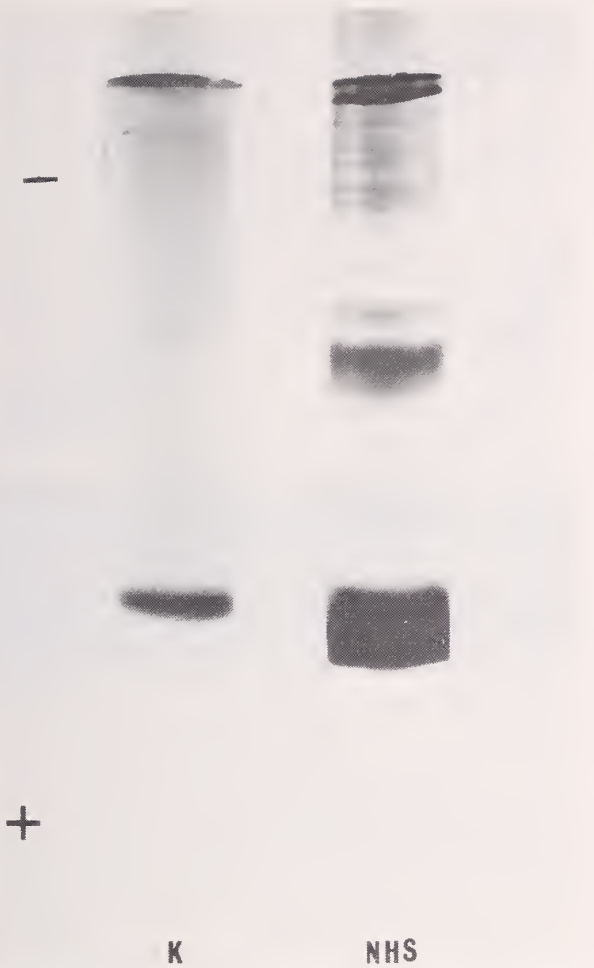

Fig. 2. Polyacrylamide gel electrophoresis of fraction K (from Fig. 1) illustrating the degree of purification.

chromatography[1] and *purified* by preparative polyacrylamide gel electrophoresis in technical conditions described in Figure 1. The degree of purification was evaluated by analytic gel electrophoresis, by immunoelectrophoresis (Figures 2 and 3) and by the criteriom of immunization by induction of a monospecific antibody (Figure 5).

The evaluation of the immunological specificity of the CPP in the fluid was made by double diffusion studies between the monospecific antibody and the following physiological and pathological fluids: normal human female serum, normal human milk, ascitic fluid, amniotic fluid, and ovarian cyst fluid. Confirmation of the specificity of *CPP for human breast cyst* fluid has further been demonstrated, as illustrated in Figure 4, by a double diffusion study where the purified protein was reacted against the anti human serum proteins antibody, the anti-breast cyst proteins antibody, the anti human normal milk antibody, the anti-ascitic proteins fluid antibody, and the anti human amniotic porteins antibody.

The binding property of CPP for progesterone was made by immuno-autoradiography with the aid of the method already used for the alphafoeto protein and described by Uriel.[3] See Figures 6a and 6b for technical data.

Cellular localization of the CPP was made by the enzyme antibody tagging method[4] in the indirect immunological system. The goat anti-rabbit gammaglobulin antibody was tagged with glucosoxydase. The control reactions were made with the normal rabbit gammaglobulin, the anti human albumin gammaglobulin fraction, and by the absorption of the specific reaction with the purified CPP. As illustrated in Figure 7, the CPP is specifically localized in the cytoplasm of canalicular cells of the cyst.

The *association of CPP with breast cancer* in a preliminary study mady by qualitative double diffusion is illustrated in Figure 8 and Table I. In fact, CPP can be detected in breast carcinoma. We have observed in 19 breast carcinoma-bearing women studies that 14 present a positive reaction.

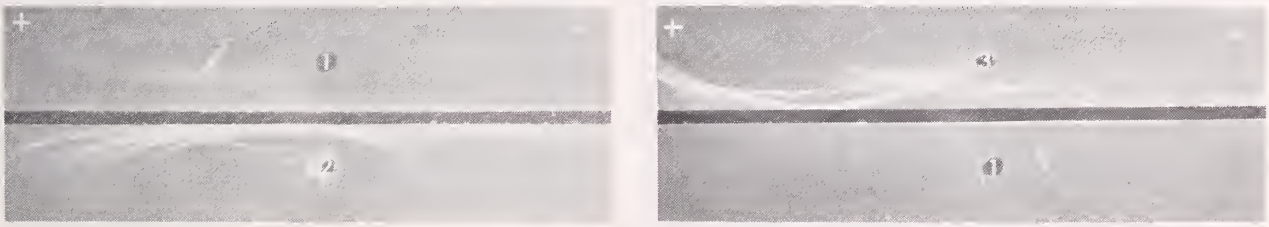

Fig. 3. Immunoelectrophoresis analysis of the purified cyst protein illustrating the α mobility (a) and the non reactivity of this protein with the normal human serum proteins antibody (b).

1) Fraction *k*
2) Breast Cyst Fluid
Antibody: Rabbit anti cyst fluid proteins

1) Fraction *k*
3) Normal human Serum
Antibody: Rabbit anti human serum proteins

Results and Discussion

This immunological study demonstrates that the CPP is highly *specific* for human breast cyst fluid and that this protein is immunologically *different* from the protein described by Haagensen[2] since there is no immunological reaction with the human milk protein. We also show that this protein has a binding property for *progesterone* and that this pro-

tein is localized in the *cytoplasm of the canalicular* cells of the breast.

On the other hand, our preliminary study gives the indication that CPP could be liberated in the serum of women with breast cancer. At this time it is impossible to make an etiological relation between this protein and the development of breast cancer.

It is also impossible to make a relation between the positive reaction and the nature of the tumor.

However, if we refer to the cellular localization of this protein in the *canalicular* cells, we can make the hypothesis that the *liberation* of this protein in the serum could be associated with tumor infiltration in this morphological region.

Thus, the detection of CPP in the serum may be a marker for cellular *infiltration* of cancer cells in the breast.

We see some interest in the detection, by im-

Fig. 4. Evaluation of the specificity of a human breast cyst fluid protein.

Central well: the purified cyst protein (k).

Peripheral wells: respectively, the following rabbit antibodies: anti human serum proteins antibody (1), anti breast cyst proteins (2), anti human normal milk proteins (3), anti ascitic fluid proteins (4) and anti human amniotic fluid proteins (5).

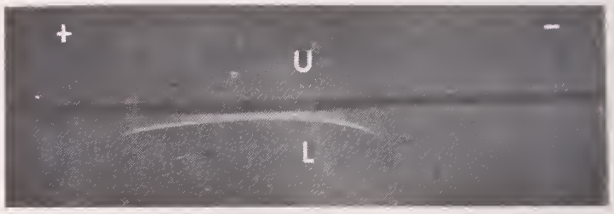

Fig. 5. Immunochemical evaluation of the degree of purity of the human breast cyst protein as evaluated by the criterium of immunization.

Upper well: Normal human serum
Lower well: Breast cyst fluid
The antibody: The rabbit anti purified (fraction *k*) cyst fluid protein.

Fig. 6a

Fig. 6b

Fig. 6. Immunoautoradiographic studies demonstrating the binding properties of the human cyst fluid specific protein for progesterone, as evaluated by double diffusion (a) and by immunoelectrophoreses (b).

Technical data: In the double diffusion study reaction was performed between the normal human serum (1), the human breast cyst fluid (2) the semi purified protein (3) and the purified specific protein (4) and the rabbit specific antibody against the cyst fluid proteins. In the immunoelectrophoretic analysis the reaction was made between the cyst fluid proteins (2) and the normal human serum (1) against the rabbit specific antibody. Incubation was made with Progesterone c^{14} (0.1ml cyst fluid incubated with 2 microcuries) for twelve (12) hours and exposed under a Kodak Regulix-HS radiographic film for one month.

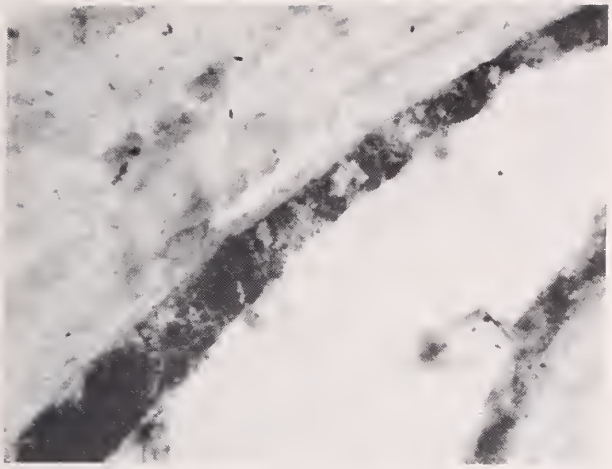

Fig. 7. Immunohistochemical localization of the CPP with the aid of the enzyme antibody tagging method.

The goat anti rabbit gammaglobulin has been tagged with glucosoxydase.

The first antibody used is the rabbit gammaglobulin fraction antipurified CPP.

Note that the human cyst progesterone binding protein is localized in the cytoplasm of canalicular cells of the cyst.

Table 1

Detection of CPP in Plasma of Women With Breast Carcinoma

Patient category	*No. of cases*	*Positive*	*Negative*
Normal adults			
Men	10	0	10
Women	10	0	10
Breast Cyst Bearers	9	1	8
Breast Carcinoma	19	14	5

munological methods, of this protein in the serum of patients with breast cancer. This could be a way to make a *molecular biopsy* for early evaluation of the degree of infiltration of cancer cells in the breast.

Fig. 8. Demonstration of the presence of the human breast cyst progesterone binding protein in the serum of a woman with breast cancer.

1. Normal human female serum.
2. Breast cyst fluid.
3. Serum of a woman with breast carcinoma.
A. Rabbit anti-purified breast cyst progesterone binding protein.

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Covenants Not to Compete in Medical Partnership Agreements — How to Avoid Some of the Problems

MARTIN L. WILK*

It is not uncommon for medical partnership agreements to contain restrictions prohibiting withdrawing or retiring partners from practicing in the community served by the partnership for a specified number of years. Such restrictive covenants, or covenants not to compete, have generally been upheld by the Courts if they (1) are reasonably limited in time and territory, (2) impose only such restraint as is necessary to protect the interests of the partnership, and (3) do not adversely affect the public interest.

While the precise question of the validity of a restrictive covenant in a medical partnership agreement has not been presented to Maine's highest court, in *Roy v. Bolduc*, 140 Me. 103 (1943), the Court refused to enforce a covenant not to compete in a contract of employment between an established real estate broker and a junior real estate salesman. The restriction in issue in that case prohibited the salesman from engaging in the real estate brokerage business in Augusta-Waterville-Skowhegan and surrounding areas for a period of five years subsequent to the termination of his employment. The Court expressed its disfavor with the covenant as follows:

> "On this record the complaining employer fails to sustain his allegations that a reasonable protection of his real estate business requires the enforcement of the restrictive agreement he obtained from his salesman. He had no trade secrets and imparted no confidential information which have or can be used to his disadvantage and there has been no interference with the customers on his lists. To restrain his employee from acting as a real estate agent on his own account, for the time and in the extensive territory included in his agreement, would unnecessarily interfere with the rightful exercise of his skill and knowledge in gaining a livelihood in what is now his calling or trade. Tested by the rules which have been stated the restriction upon the employee's liberty of action, which is written into the contract of employment in this case, is against public policy and equity will not enforce it." 140 Me. 103 at 108.

Whether the Court's attitude would have been the same if the covenant had applied to the members of a medical partnership is difficult to predict. Such a broad restriction may well have been stricken down even if it had been knowingly and voluntarily entered into by parties of equal bargaining power engaged in the practice of medicine. Even a more narrowly drawn restriction would not be immune from attack. Indeed, if current attitudes of the Courts with respect to other traditional anticompetitive arrangements such as uniform fee schedules and bans on professional advertising are any guide, the days of the restrictive covenant, however limited, could be numbered.

The outcome of any case challenging the enforceability of a covenant will, of course, depend upon the specific language of the covenant as well as the particular factual context in which the challenge arises. While there is no precise formula for determining what a court will consider reasonable and what a court will find offensive, there are a number of common pitfalls that should be avoided.

- *Be sure to specify a time period.*

Cases have arisen where the covenant specifies a geographic territory, but fails to mention any time period limiting the duration of the restriction. Some courts have held that where no time period is stated expressly, a reasonable period will be implied. Others have ruled that the absence of a stated period means that the restriction was intended to be of unlimited duration and concluded that such a restriction was unlawful.

- *Limit the time period as much as possible.*

The Courts have upheld agreements not to compete for a period of 3 years, 5 years and even 10 years. However, the longer the term of the restriction imposed, the more difficult the covenant usually is to justify.

- *Be sure to specify a geographic territory.*

Cases have arisen where the covenant appears reasonably limited in time, but silent as to territorial application. In such circumstances some courts have implied a reasonable territory, while others have declared that the failure to specify any geographic territory renders the covenant unlawful.

- *Limit the territory as much as possible.*

The Courts have upheld restrictions that extend

*Mr. Wilk is a member of the law firm of Wilk & Scott, Augusta, Maine. He is a former Deputy Attorney General for the State of Maine.

to an entire town, a village, a city or even one or more counties. The Courts have also upheld restrictions that define the applicable territory in terms of a radius of miles (10, 50 or even 100 miles) from a particular location. Again, however, the broader the territory embraced by the agreement not to compete, the more difficult the restriction usually is to justify. As a rule of thumb, the territory specified in the covenant should be no broader than the area actually served by the partnership.

• *The covenant should apply equally against all partners of relatively equal position in the firm.*

Oftentimes the covenant is drawn so that it operates only against one or more younger members of the partnership. As the relationship of these members to the partnership matures, and the value of their services to the partnership increases, the more difficult it may become to justify disparate treatment under the covenant. As a rule of thumb, equal partners should be treated alike.

• *Be cautious of covenants that take effect involuntarily.*

The covenant is often drawn so that it only takes effect upon voluntary withdrawal or retirement from the partnership — that is, when a partner decides for himself to leave the partnership. Other times the restriction is drawn so that it takes effect upon termination of a partner's interest involuntarily; for example, when a partner is dismissed against his will.

In either situation, it is important to remember that the restraint may not be any broader than is necessary to protect the valid interests of the partnership or the remaining partners. If a junior partner who has spent only one or two years in the partnership decides to leave and establish his or her own practice in the community, the partnership or the remaining partners may have a valid interest in prohibiting the newcomer from luring away patients that have been cared for by the partnership long before he or she arrived on the scene.

On the other hand, the equities of the situation would be quite different if the newcomer moved into the community at the request of the partnership, and wished to remain a partner, but was dismissed against his will. The matter could become even more troublesome if the newcomer had a basis for maintaining that he or she had served the partnership in good faith, had contributed to the partnership's financial well being, and had been dismissed unfairly. A Court may be less tolerant of a covenant not to compete under these facts, than in the voluntary withdrawal situation.

• *Consider the impact of the covenant upon the medical needs of the community.*

While there has been no reported case to date where a covenant not to compete has been declared invalid solely because of its impact on the medical needs of the community, the Courts appear to be devoting more attention to this factor now than in earlier cases. Public policy arguments against a restrictive covenant would take on added strength where the effect of enforcing the restriction would be to place a severe strain on the availability of required medical services in a particular area.

Following the foregoing suggestions will not insure that the restrictive covenant in your partnership agreement will withstand a court challenge. Nor will they insulate you from the internal problems and frictions that can arise where agreeing to a covenant not to compete is a precondition to joining a partnership.

One solution to avoiding these problems is, of course, to refrain from utilizing anticompetitive restrictions entirely. Interestingly, the use of such covenants is considered unethical in the legal profession. If lawyers have managed to get by without such restrictions, perhaps doctors can as well.

THE FUTURE OF THE PRIVATE HEALTH SYSTEM

The following is an excerpt from a speech given by Lance Hoxie of the Blue Shield Association at a Maine cost containment meeting.

The future of a private health care delivery system depends largely upon us. Failure on the part of physicians and carriers to accept responsibility in curbing rising costs could result in consequences none of us are prepared for.

We share one principal goal: that is to provide the American people with the best possible health care; to maintain the health of the healthy and to care for the sick. This is the reason for the existence of the medical profession. Blue Shield was founded — and exists today — to assure that people can afford the health care they need. All of our technology, physician supply and hospital care require an adequate economic base. Without it, they can't become useful enough to pose a cost problem.

The health care system should put far greater premium on explaining the underlying causes of health cost to the public. When expectations about health cost are reasonable, we can do more to meet those expectations.

Resources of the health care system must be used in the most economic manner to achieve the objective of the best possible health care. "Best Possible" does not imply most extravagant; does not imply the use of all possible modalities. It should imply cost efficiency as a significant factor in the decision process. If we can get to that, we should be able to establish realistic objectives to accommodate expanded capacity and inflation in a rational, predictable way.

The medical profession, the health care financing industry — the whole health care system — suffers in part from its own failure to communicate to the American people. We have been so intent upon improving the services and products we provide people that we failed to communicate our progress to those people. Instead, many physicians, hospitals and carriers have simply abandoned debate to the critics. We have a story to tell and we had better tell it.

We need to explain the complexities of the health care industry. We need to educate the public about the ramifications of the various legislative proposals to federalize health insurance.

The cost of health care more than any other health care issue could be the principal reason for diluting the public's faith in private financing of health care and moving the industry under the federal government.

Our performance as cost controllers will have great impact on our future. We must attack areas of weakness and waste head on.

Physicians will have to practice medicine with an awareness of the ceiling on health care resources and dollars.

The proliferation and redundancy of equipment and technology must be controlled.

Our efforts so far have not been in vain. They've all been productive and we have been able to document the dollars saved.

With continuing effort, we can remain the best health care providers in the world.

The facts prove that we have done — and are doing — a good deal to test, research and utilize effective methods to meet all the health care needs of our subscribers and patients.

County Society Notes

Continued from Page III

President: Dr. James F. MacMahon, Farmington
Secretary-Treasurer: Dr. Daniel K. Onion, Farmington
Delegate to the M.M.A. House of Delegates: Dr. David S. Hurst, Farmington. Alternate: Dr. Gaetano T. Fiorica, Jay

3. *Discussion of West Central Maine Health Services by Dr. N. Burgess Record, Jr.* (hour discussion) — A committee to work as a liaison between the Franklin County Medical Society and West Central Maine Health Services was elected which consists of Drs. Paul A. Brinkman, Christopher S. Smith (non-member), Gretl J. Hoch, H. Wilson Eastman and Chet Mitchell, D.O. (non-member).

The Franklin County Medical Society met on October 10, 1977.

The meeting was called to order by the President, Dr. James R. MacMahon.

Items of Business:

1. Dr. MacMahon announced the new State laws regarding immunizations and admittance to schools.

2. Dr. Onion reported on Medical Society activities, regarding 1) Certificate of Need legislation, 2) Health and Welfare suit by the Medical Society regarding physician reimbursement, and 3) Dr. Hanley's request for membership on an arbitration panel.

DANIEL K. ONION, M.D., *Secretary*

Hancock

The Hancock County Medical Society met at the Hilltop House in Ellsworth, Maine on November 2, 1977.

The meeting was called to order by the President, Dr. John D. McIntyre, and the minutes of the previous meeting were reviewed and approved.

Items of new business, as brought up by Dr. McIntyre, were as follows:

1. Professional Competence Committee — The function of this committee as mandated by State laws was discussed. It was moved by Dr. Elizabeth E. Williamson that the officers of the Society compose this committee. This motion was seconded by Dr. John R. Tyler. This motion was unanimously approved and then a motion was made by Dr. Russell G. Williamson, also seconded by Dr. Tyler, to rescind the above motion as there might be conflicts with the present bylaws in regard to the present censor's committee. This motion was likewise unanimously approved and subsequently a new motion was made by Dr. Russell Williamson and seconded by Dr. Elizabeth Williamson that the officers of the County Society be designated as the censors committee — that is, President, Vice-President, and Secretary — and that therefore this committee would then also serve as the Professional Competence Committee. This motion was likewise unanimously approved.

2. The matter of physicians being designated as medical malpractice arbitrators in accordance with the Maine Health Security Act. The following members agreed to serve in this capacity: Drs. Robert W. Suscy, Randall H. Silver, John D. McIntyre, Quinby D. Gurnee, Eji Suyama, Russell G. Williamson and Robert W. Milam (non-member, presently in the process of applying for membership).

3. Certificate of Need Legislation. Attention was called to the group in regard to this legislation and, in particular, members were encouraged to write and call legislators, as well as attend the meeting of the Committee of Health and Institutional Services to be held on November 15 at the State House in Augusta.

4. A letter from Dr. Melvin Bacon regarding the State Diabetes Committee was read. It was the concensus of the group that each hospital in this area provide its own local programs in diabetes detection and education and therefore no local society chairman was deemed necessary.

There being no further business, the speaker of the evening was introduced, Dr. Kenneth McKerns, former professor of endocrinology at the University of Florida. His topic was "Potential New Methods in Contraception" and he gave a fascinating presentation of new hormonal modifications and cellular level approaches to contraceptive problems.

The meeting was adjourned at 9:25 p.m.

WILLIAM C. BROMLEY, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association met at Guido's Wine Cellar at Augusta on October 20, 1977 with 30 members in attendance compared with 31 for the comparable date in 1976.

The meeting was called to order at 8:00 p.m. by the President, Dr. Richard E. Barron, following a very nice dinner.

The following correspondence was read: A letter of resignation from Dr. Percy C. McIntyre which was accepted by the Council; correspondence from the Medical-Legal Liaison Committee of the Maine Medical Association regarding the Malpractice business.

New business: The applications of Drs. Neil Newton, Edward Salmon and Joseph Houle were read.

Old business: The applications of Drs. Stephen M. Becker and Paul Hermann were voted on and they were accepted into membership.

Following the business meeting, Dr. Barron introduced our speaker, Dr. Robert I. Roy, one of our own members, who presented a most informative discussion of the current status of total joint replacements, emphasizing the hip and the knee.

The meeting was adjourned at 9:30 p.m.

The Kennebec County Medical Association met at the Silent Woman in Waterville, Maine on November 17, 1977, with 40 members and two guests in attendance. Following a nice meal, the President, Dr. Richard E. Barron opened the meeting at 8:00 p.m.

Correspondence: A request from the Maine Medical Association for physicians willing to serve on the malpractice panel was read by Dr. Barron. A letter to the family of Dr. Napoleon J. Gingras was entered into the records.

New Business: The application of Dr. H. Winstop Kipp was read.

Old Business: Applications of Drs. Neil A. Newton, Joseph A. Houle and Edward L. Salmon were voted upon favorably.

Further New Business: Dr. Gareth O. M. Jones raised the question of the differentials and medicare fee schedules around the county and requested the members of the Association to vote that the Maine Medical Association and the delegates to the AMA be requested to affirm the stand that Maine physicians were not second class citizens and to seek for a more equitable fee schedule for Maine physicians. The members of the Association voted in favor of this concept. The secretary was requested to inform the Maine Medical Association of this action.

Dr. Barron then introduced Mr. Chester Dosdall of the Joint Underwriting Association who gave a most informative presentation of the function of the JUA. A very active discussion was held.

The meeting adjourned at 9:00 p.m.

O. THOMAS FEAGIN, M.D., *Secretary*

Knox

The Knox County Medical Society met at the Sail Loft Restaurant in Rockport on October 4, 1977.

Dr. Alta Ashley stated that the helicopter service from Monhegan Island is currently being routed to Boothbay and questioned the possibility of it being routed to Pen Bay Medical Center. This issue was referred to Dr. Johan Brouwer.

Dr. Douglas R. Hill, President of M.M.A., spoke regarding the Questionnaire on Malpractice Insurance. He encouraged return

by physicians to determine whether it is feasible to set up a State-wide malpractice company.

He discussed the lawsuit in Federal Court that was initiated by M.M.A. to challenge the 10% cut in doctors' medicaid fees legislation.

M.M.A. is challenging the concept of "certificate of need" as it has been applied to private M.D.'s offices.

He informed the members that a newsletter will be sent to individual members to update them on matters facing the legislature to help them influence local legislators.

Drs. Peter R. Shrier and Albert J. Lantinen spoke on "Post-Menopausal Estrogens."

There being no further business, the meeting was adjourned.

JACK D. MCCUE, M.D., *Secretary*

Lincoln-Sagadahoc

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held at the Ledges, Wiscasset, Maine on November 15, 1977. There were thirty members and guests present.

The President, Dr. Anthony J. Horstman, called the meeting to order at 8:20 p.m.

The minutes of the September and October meetings were read by the Secretary and accepted as read.

There was no old business. Dr. Horstman then read applications for active membership from Drs. Andrew D. Cook of Brunswick, John R. Vinton of Damariscotta, and Mary Ann Chase of Damariscotta. The applications were recommended by the Board of Censors and were accepted unanimously.

Dr. Bostwick recommended that 1978 dues be the same as 1977 dues: $40.00. The vote was affirmative.

Dr. Horstman appointed Drs. David W. Schall, Frank O. Avantaggio, Jr. and Charles E. Burden as a Nominating Committee to bring in a prospective slate of officers for 1978 for vote at the annual election in December.

Dr. Elihu York then introduced Dr. Edward Nowicki, of Portland, who spoke on open-heart surgery at the Maine Medical Center. Discussion of coronary artery bypass surgery followed.

The meeting was adjourned at 10:00 p.m.

GEORGE W. BOSTWICK, M.D., *Secretary*

Oxford

A regular meeting of the Oxford County Medical Society was held on October 12, 1977 at the Bethel Inn in Bethel, Maine, with twelve members present.

The meeting opened under the direction of Dr. Adwaita K. Ganguli, President, Rumford, Maine.

Minutes of the last meeting were read and approved.

Election of officers for the ensuing year:

President: Dr. Kenneth G. Hamilton, Norway

Vice-President: Dr. H. Richard Bean, Norway

Secretary-Treasurer: Dr. Harbans S. Sodhi, Norway

Councillors: Drs. Stephen B. Dewing, Harrison and Sidney M. Schnittke, Rumford

Dr. David L. Phillips, Rumford, reviewed the present membership of the Society.

The Society commended the Maine Medical Association for the initiative in filing the legal suit to protect the interest of the members of the Society.

HARBANS S. SODHI, M.D., *Secretary*

Penobscot

The first meeting of the 1977-78 season of the Penobscot County Medical Society was held on October 18, 1977 at the Heritage Inn in Millinocket, Maine.

The meeting was opened by the President, Dr. Philip G. Hunter and the minutes of the annual meeting from May 1977 were discussed and accepted. With the institution of a monthly newsletter beginning this month, information regarding the annual meeting of the Maine Medical Association in Rockport last June and various legislative proceedings during the summer have been previously made available to the membership and was not further discussed other than particular questions on any of the various topics covered in the newsletter. The plans are to continue this newsletter on a monthly basis while the Society is meeting between October and May.

Under new business, Dr. Hunter reminded the membership to be sure they returned the questionnaire from the firm of Johnson & Higgins of Boston who is conducting a study to determine the feasibility of a captive professional liability insurance company for Maine doctors. He reminded us that the JUA is only a temporary measure in alleviating the current malpractice crisis. Fourteen applications for membership were presented; seven of these were for full membership and seven were for junior membership (Family Practice residents at EMMC). All fourteen were unanimously accepted. The doctors accepted into full membership are Drs. Denis F. J. Halmagyi, Cressey W. Brazier, Douglas M. Sewall, James F. Izzard, Donald W. Krause, Patrick W. Kamm and Henry H. Atkins, II; junior members accepted are Drs. Daniel Rissi, Stephen I. Levine, Richard H. Emmons, George K. Dreher, Jr., Robert A. Fleury, Christopher Ritter and Judith Chamberlain.

Drs. Frank Padberg and David Sizemore from the Nutritional Support Service of the New England Deaconess Hospital in Boston then presented a most enlightening illustrated talk of the nutritional and metabolic assessment of the hospitalized patient and indications and techniques for parental hyperalimentation.

There being no further business, the meeting was adjourned at 11:00 p.m.

H. CLEMENT JURGELEIT, M.D., *Secretary*

Washington

A regular meeting of the Washington County Medical Society was held in the Conference Room of the Calais Regional Hospital, Calais, Maine on November 17, 1977, with eight members present.

I. Reading of minutes of last meeting, read, discussed and approved.

II. *Old Business:*

a) Considerable discussion of the Certificate of Need Legislation with a report that the legislation pertaining to physicians was still pending and would need further action by physicians.

b) Physicians present were urged to contact members of the Joint Committee on Health Institutional Services.

1) Dr. Donald M. Robertson stated that he would find out who attended the first session of this Joint Committee and the names of those voting for and against this legislation and so notify us.

III. *W.C.H.P.:*

Dr. Robert G. MacBride, member of the Washington County Health Plan, Board of Directors, reported on the WCHP. He stated that they appeared to have a very dedicated and interested board. They were in the process of setting up new contracts to send out to physicians. He stated that he was a member of a Provider Relations Committee that hopefully would meet with physicians.

a) A motion was made by Dr. Robert G. MacBride that a committee from WCMS be set up to discuss matters of mutual concern with a comparable committee for the WCHP or similar organizations. This committee to accumulate facts to report back to the WCMS before a definitive action be taken. Members of this committee to be appointed by the chair.

1) This motion was seconded and passed, by members present; however, before it can be fully approved, it is necessary that this be voted on by ballot, by all members of the WCMS.

IV. *Discussion of Down East Health Service:*

a) Dr. Randall H. Silver reported on the various activities of the DEHS and stated that it appeared to be functioning well, at present.

V. *Dues:*

It was voted to double the dues of the Washington County Medical Society.

VI. *House of Delegates:*

The two (2) members present at the meeting Drs. Donald M.

Continued on Page 31

Robertson and Robert G. MacBride were asked to present certain matters of interest to the House of Delegates and report back at the next meeting.

VII. *Malpractice:*

Discussion of Malpractice and the differences in cost between different insurance companies.

VIII. *Arbitration:*

Arbitration panel discussed. No action.

IX. *National Guidelines:*

National guidelines as to health planning discussed.

X. *Fee Schedule:*

Discussion of fee schedule with the feeling that a profile was still in effect. It was noted that there was no added fee for calls after midnight. Dr. James C. Bates said that he would write and find out the reasons why this was not included and would try to see if changes could be made to have this included.

XI. The Society decided to invite a speaker down to explain the various ramifications of Malpractice Insurance and whether it would be to our benefit to be further involved.

XII. The next meeting to be Thursday, January 19, 1978 at the Peavy Memorial Library, Eastport, Maine.

KARL V. LARSON, M.D., *Secretary*

News, Notes and Announcements

State of Maine
Department of Human Services
Division of Child Health Clinic Schedule — 1978
By Appointment Only

Orthopedic Clinics

Bangor — St. Joseph Hospital
9:00 a.m.: Jan. 26, Feb. 23, Mar. 23, Apr. 27, May 25, June 22, July 27, Aug. 24, Sept. 28, Oct. 26, Nov. 16, Dec. 14

Fort Kent — Northern Maine Medical Center
9:00 a.m.: Mar. 14, May 9, July 11, Sept. 12, Nov. 14

Houlton — Houlton Regional Hospital
10:00 a.m.: Mar. 13, May 8, July 10, Sept. 11, Nov. 13

Lewiston — Central Maine Medical Center
Orth., 9:00 a.m.: Feb. 17, Apr. 21, June 16, Aug. 18, Oct. 20, Dec. 15. Scol., 9:00 a.m.: Jan. 20, Feb. 17, Mar. 17, Apr. 21, May 19, June 16, July 21, Aug. 18, Sept. 15, Oct. 20, Nov. 17, Dec. 15

Presque Isle — A. R. Gould Memorial Hospital
9:00 a.m.: Mar. 15, May 10, July 12, Sept. 13, Nov. 15

Waterville — Mid-Maine Medical Center (Thayer Unit)
(Time scheduled by hospital): Feb. 6, Mar. 6, Apr. 3, May 1, June 5, Sept. 11, Oct. 2, Nov. 6, Dec. 4

Cleft Palate Clinic

Portland — Maine Medical Center
9:00 a.m.: Feb. 13, May 15, Sept. 18, Nov. 20

Cardiac Clinics

Bangor — St. Joseph Hospital
9:00 a.m.: Feb. 10, Mar. 10, Apr. 14, May 12, June 9, July 14, Aug. 11, Sept. 8, Oct. 13, Nov. 17, Dec. 8

Portland — Maine Medical Center
9:00 a.m.: Jan. 20, Feb. 3, 10, 17, Mar. 3, 10, 24, Apr. 7, 14, 21, May 5, 12, 19, June 2, 9, 16, 30, July 7, 14, 21, Aug. 4, 11, 18, Sept. 1, 8, 15, 29, Oct. 6, 13, 20, Nov. 3, 17, Dec. 1, 8, 15, 29

Children's Development Clinics

Lewiston — Central Maine Medical Center
8:30 a.m.: Feb. 13, Mar. 13, Apr. 10, May 8, June 12, July 10, Aug. 14, Sept. 11, Oct. 23, Nov. 13, Dec. 11

Waterville — Mid-Maine Medical Center (Thayer Unit)
8:30 a.m.: Feb. 1, Mar. 15, Apr. 5, 19, May 3, June 7, 21, July 5, Aug. 16, 30, Sept. 6, 20, Oct. 4, Nov. 1, Dec. 6

Education Programs — 1978
Goodall Hospital, Sanford, Maine

Thursday, January 19

Speaker: Stuart Schlosman, M.D., Sidney Farber Institute, Children's Hospital, Boston, Massachusetts
Subject: "Diagnosis and Treatment of Blood Dyscrasias"

Tuesday, February 21

Speaker: Harold Simon, M.D., Newton Wellesley Hospital, Newton, Massachusetts
Subject: "Ultra-Sound — Its Diagnostic and Therapeutic Application"

Thursday, March 16

Speaker: Jan Drewry, M.D., Director, Division of Nephrology, Maine Medical Center, Portland, Maine
Subject: "Fluid and Electrolyte Balance"

Tuesday, April 18

Speaker: Richard W. Erbe, M.D., Chief, Genetics Unit, Children's Service, Massachusetts General Hospital, Boston, Massachusetts
Subject: "The Role of Genetics in Medicine"

Thursday, May 18

Speaker: Johanna Dwyer, M.D., Francis Stern Nutritional Center, New England Medical Center, Boston, Massachusetts
Subject: "The Use and Abuse of Dietary Regimes — What Constitutes the Normal Diet"

Tuesday, June 20

Speaker: Paul M. Cox, M.D., Director, Intensive Care Unit, Maine Medical Center, Portland, Maine
Subject: "Current Thinking in Shock"

These meetings are held in the Conference Room of the Goodall Hospital at 7:00 p.m. on the dates indicated and are accredited by the American Academy of Family Practice for two hours, for each meeting.

Harvard University Announces Two Executive Education Programs In Health Management To Be Offered In 1978

The seventh Program for Health Systems Management will be conducted from June 18 to July 28, 1978. The Program is designed for experienced, senior managers in health delivery and health-related organizations. Applications are due on March 15.

The second Management Development Program in Health will be conducted in two coordinated segments. The first segment will be offered April 2-20, 1978 and the second segment, September 10-29, 1978. To complete the Program, participants are required to attend both segments. The Program is designed for mid-level managers in health delivery and health-related institutions and for functional managers who are moving, or have recently moved, into general management positions. Applications are due on February 7.

Both programs are designed to expand the managerial and problem-solving skills of the participants and to broaden their understanding of the management problems facing institutions throughout the health system. The Harvard Business School's

well-known case method of instruction, which actively involves participants in problem analysis and decision making, encourages the exchange of viewpoints among participants from diverse geographic and organizational settings in the public and private, for-profit and voluntary health sectors.

Participants in each Program differ primarily in terms of the level of their managerial responsibilities and the number of years of their managerial experience. The curricula of the two Programs differ insofar as they are designed to address the needs of executives at different stages in their career development. The Programs include courses in financial management, marketing management, control, health economics, legal issues, organizational issues, health services, operations management, labor relations, and institutional policy and strategy.

The Programs are offered under the administrative auspices of the Office of Executive Programs in Health Policy and Management at the Harvard School of Public Health. The experienced, interdisciplinary faculty have been drawn from the Harvard graduate schools of Public Health, Business and Medicine.

As a matter of policy, Harvard University does not discriminate on the basis of race, sex, or handicap. Qualified women and minority group members are strongly encouraged to apply.

Applicants must be sponsored by their employer organizations, which are responsible for the program fees that cover instruction, materials, room and board, and activities. Inquiries should be addressed to: Administrative Director, PHSM/MDPH, Executive Programs in Health Policy and Management, Harvard School of Public Health, 677 Huntington Avenue, Boston, MA 02115.

Institute For Sex Research
Ninth Annual Summer Program In Human Sexuality
June 21-28, 1978

Lectures, panel discussions, audiovisual materials, and attitude reassessment workshop covering sex behavior, sex therapy, and current sociosexual issues. Courses designed for individuals in the health professions and other professional fields. Conducted by ISR staff and distinguished guest lecturers.

Registration fee $325.

Contact: Institute for Sex Research — Summer Program, 416 Morrison Hall, Indiana University, Bloomington, IN 47401.

Letters to the Editor

To the Editor:

The Massachusetts Medical Society, upon the recommendation of Dr. Bradley E. Copeland, head of the clinical laboratories at the New England Deaconess Hospital, has, through its Council (legislative body) taken a stand on the subject of what system of recording the results of clinical chemistry tests should be used. Its stand is that the use of mass concentration units (mass-weight/volume) should be retained in all the medical laboratories in the state until it can be shown that a change to mole concentration units will improve patient care through better diagnosis, treatment and follow-up and that it would provide a significant advantage in respect to laboratory measurement techniques. It also has expressed itself strongly in favor of having practicing physicians thoroughly involved in any discussion which leads to change.

I am sending this information to you and your medical society to stimulate thought on this subject and with the hope that perhaps your members might wish to take similar action.

John J. Byrne, M.D.
President
The Massachusetts Medical Society
22 The Fenway
Boston, MA 02215

Tablets
Percocet®-5 CII

DESCRIPTION Each tablet of PERCOCET®-5 contains 5mg oxycodone hydrochloride (WARNING: May be habit forming), 325mg acetaminophen (APAP).

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone or acetaminophen.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCOCET®-5, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCOCET®-5 is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCOCET®-5 should be cautioned accordingly.

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCOCET®-5 may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCOCET®-5 should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCOCET®-5 should not be administered to children.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions The administration of PERCOCET®-5 or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients PERCOCET®-5 should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. PERCOCET®-5 is given orally. The usual adult dose is one tablet every 6 hours as needed for pain.

DRUG INTERACTIONS The CNS depressant effects of PERCOCET®-5 may be additive with that of other CNS depressants. See WARNINGS.

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November 1977 EDO 148P

The Journal of the Maine Medical Association

Volume Sixty-nine | Brunswick, Maine, February 1978 | Number 2

Unusually Long Survival of Patients With Cancer*

LORING W. PRATT, M.D., F.A.C.S.**

This paper is presented to raise a question rather than to answer one. Many have seen patients who have made unusually long survival though living in association with malignancy. The Author has been privileged to be associated with the care of two patients who have enjoyed survival of unusual duration, whose cases are reported here to raise questions about the nature of cancer and the host reaction to malignancy.

Both patients are men. Both were seen for the first time in 1959, and each had carcinoma of the pyriform sinus. At this time, the anticipated five-year survival was twenty to twenty-five percent for this lesion. Each developed metastases in the neck and had intermittent recurrences of metastatic disease over the course of several years. Ultimately they ceased having recurrences, are alive, well and free of disease with no evidence of recurrent tumor during the past seven years.

Considerable work has been done in recent years studying the development of the immune process in association with malignancy. BCG therapy has been used to enhance the immunological state of the individual and immunological manipulations have been attempted in order to enhance the immunocompetent state. So far this has met with only partial success, but the hope is that this will become a more effective method of treatment, when better understanding of the fundamental process has been achieved.

PATIENT #1

September 1959

First seen. Patient, age 50 years. Heavy smoker and heavy drinker. Impression ? of carcinoma of left pyriform sinus with metastasis to neck.

Laryngoscopy and biopsy. Pathology report: epidermoid carcinoma, Grade III.

November 1959

Cobalt radiation therapy — 7,500 R.

April 1960

Irradiation failure.

May 1960

Partial pharyngectomy, laryngectomy, cervical esophagostomy, left hemithyroidectomy and left neck dissection. Large pharyngostome. Physician reports, "Actually there were two separate cancers, one in the postcricoid area and the other on the aryepiglottic fold."

July 1960

Closure of pharyngostome.

April 1966

Resection of left lung, upper lobe. Pathology report: metastatic carcinoma, possibly of renal origin.

September 1967

Excisional biopsy of mass of neck. Pathology report: Mass from region of chin: metastatic epidermoid carcinoma, Grade III.

Resection of area of esophagus and skin. Reconstruction of esophagus.

January 1971

Recurrence in base of tongue and hypopharynx. Extensive ablative procedure. Pharyngoesophagectomy and esophagostomy with reconstruction.

Patient stopped smoking after this surgery.

October 1977

No evidence of disease.

PATIENT #2

December 1959

First seen. Patient, age 49 years. Heavy smoker and heavy drinker. Impression: ? cancer of larynx.

Bronchoscopy and laryngoscopy with biopsy left vocal cord and ventricle. Pathology report: Epidermoid carcinoma, Grade III.

Laryngectomy. Pathology report: Larynx: Epidermoid carcinoma, Grade III.

March 1962

Mass removed from right side of neck. Pathology report: Cervical lymph node: metastatic epidermoid carcinoma, Grade II to III.

Right radical neck dissection. Pathology report: lymph node from jugular area: Metastatic epidermoid carcinoma, Grade III.

*Presented at the First Annual Fitz-Hugh Symposium, University of Virginia, Charlottesville, VA, June 19, 1977.

**Chief, Section of Otolaryngology and Maxillofacial Surgery, Mid-Maine Medical Center, Waterville, Maine 04901.

August 1962

Exploration of neck, partial esophagectomy. Pathology report: Portion of esophagus: recurrent epidermoid carcinoma, Grade II to Grade III.

September 1962

Closure of pharyngostome.

January 1965

Mass lower left neck excised. Pathology report: Metastatic poorly differentiated squamous cell carcinoma.

May 1965

Excision of mass, left upper neck. Pathology report: Mass from salivary gland: Epidermoid carcinoma, Grade III to Grade IV.

June-July 1965

Cobalt therapy: 5,300-5,900 R.

September 1967

Left radical neck dissection. Pathology report: Well differentiated squamous cell carcinoma.

November 1967

Mass from root of neck excised: Pathology report: purulent debris and granulation tissue.

Patient stopped smoking after this surgery.

October 1977

No evidence of disease.

Long term survival of cancer patients with head and neck cancer is statistically related to their smoking habits. In the two patients studied in this paper, it is of interest to note that each man stopped smoking completely after his last surgical procedure. Forty percent of the patients who continue to smoke develop second cancers in the tobacco contact tissues and 6% of the patients who stop smoking develop second cancers.

It is interesting to speculate about the cause of the unusually long survival of these two men in the presence of frequently recurring metastases from head and neck cancer. These patients are representative of a group of individuals in whom the ability to develop immunity to malignancy did exist, this immune state developing slowly over a period of several years. It is doubtful that surgery cured the malignancies in either case; but the persistent and unrelenting surgical/radiotherapeutic attack on each recurrence of tumor possibly provided the patient with time to develop immunocompetence so that he could thereafter adequately defend himself against tumor. Reduction in the volume of the tumor by surgical excision may have facilitated the successful development of the immune state.

The exact nature of this immunological process is not well understood, but it seems clinically that this is the protective mechanism which accounts for the prolonged survival of these patients.

It is well known that recurrences of head and neck malignancies are most frequently local, and appear in the neck region. Often at autopsy, the uncontrolled tumor is confined to this very region. It is this observation and the clinical course of the patients reported above which suggests that it is essential to treat each recurrence of tumor with vigor, in order to provide local control of the tumor until the hoped for development of immunocompetence occurs, as it does in some patients.

References

Moore, C.: Smoking and Cancer of the Mouth, Pharynx and Larynx. *JAMA* 191: 283-286, 1965.

Moore, Condict: Cigarette Smoking and Cancer of the Mouth, Pharynx, and Larynx, A Continuing Study, *JAMA* 218: 553-558, Oct. 25, 1971.

Spring Meeting of the M.M.A. House of Delegates

Saturday, March 18, 1978

12:30 P.M. — Registration: 1:00 P.M. — Lunch: 2:00 P.M. — Meeting

9:30 A.M. — Meeting of the Executive Committee

Annual Meeting Dates For Your 1978 Calendar . . .

Maine Medical Association, June 10-13

Treadway-Samoset, Rockport, Maine

American Medical Association, June 17-22

St. Louis

PATIENT PACKAGE INSERTS: A CONCEPT WHOSE TIME HAS COME?

The consumer's right to know is an irreversible and desirable trend of the Seventies. It extends, and properly, to a patient's right to know more about his or her prescription medications. One way, gaining favor, is through patient package inserts. Wisely-prepared and properly distributed when medically indicated, they could markedly improve patient knowledge and drug therapy—laudable goals by anyone's standards.

The PMA endorses these goals and will work with government, the health professions and consumers to achieve them.

The Advantages

The concept holds promise of benefits: better patient understanding of the product prescribed, better adherence to the treatment plan, and more awareness of possible side reactions.

Every doctor has had patients who fail to finish antibiotic regimens because they feel better. Some patients assume that if one tranquilizer or analgesic is good, two may be twice as good. Still others fail to report dizziness while on antihypertensive therapy —and so on.

Problems like these might arise less often if the patient received written information in addition to verbal instructions. Some studies suggest that patients are more receptive to such materials, and they more often understand the verbal instructions and follow them, when inserts are used.

The Disadvantages

There are also some potential problems. Obviously, the inserts must be clearly phrased, without extraneous or complex detail. How much information is enough? How can it be kept current? Should all patients receive the same information? Should inserts be included with all drugs? Should only potential problems be listed or are patients better off with a "fair balance" presentation that describes usefulness as well as drawbacks?

These and similar questions require answers, since model inserts have yet to be properly developed and tested. Despite the need for these studies, the FDA is proceeding prematurely with inserts on selected products. We think the Congress is the only place where the matter can be given the proper legal status and direction, particularly since it represents a conceptual change in the legal, medical and social framework of the nation's prescription drug information system.

The Solution

The PMA believes that carefully-devised pilot studies of various kinds of inserts are needed. They should be developed and implemented with full participation by doctors, pharmacists, consumers, communications experts and the drug industry. Such studies will provide reliable pathways to follow, so that inserts will be useful aids to medical practice.

And particularly we think that you should be closely involved in this debate and in these studies and decisions. Otherwise, people with less experience and qualifications may control the purposes, content and use of a tool with considerable promise for improved patient care. It could make a difference in your practice tomorrow, and more importantly, in the health of your patients.

PMA

THE PHARMACEUTICAL MANUFACTURERS ASSOCIATION
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Basic Pulmonary Function Testing

(What It Means and How to Use It)

IRVIN PARADIS, M.D.*

INTRODUCTION

Patients with a variety of pulmonary disease complain of cough and shortness of breath more than any other symptom. Physiologic tests, developed for the quantitative evaluation of respiratory function, have proven to be useful in the diagnosis and guidance of therapy for patients with many respiratory disorders. These pulmonary function tests may reveal abnormalities early in the course of disease when clinical and roentgenologic examinations are still normal. Although such tests indicate how function has been altered by disease, they cannot determine either the etiology or the pathology causing the abnormality. For example, a test may indicate a restrictive defect, but it cannot differentiate between restriction from pulmonary fibrosis or from a previous pneumonectomy.

Occasionally multiple types of pulmonary function tests are required to properly characterize a patient's abnormalities. More frequently, however, a properly performed expiratory spirogram with a thorough history and physical examination will yield the information necessary to arrive at a diagnosis. This discussion will devote itself to the use and interpretation of this test because it contains a

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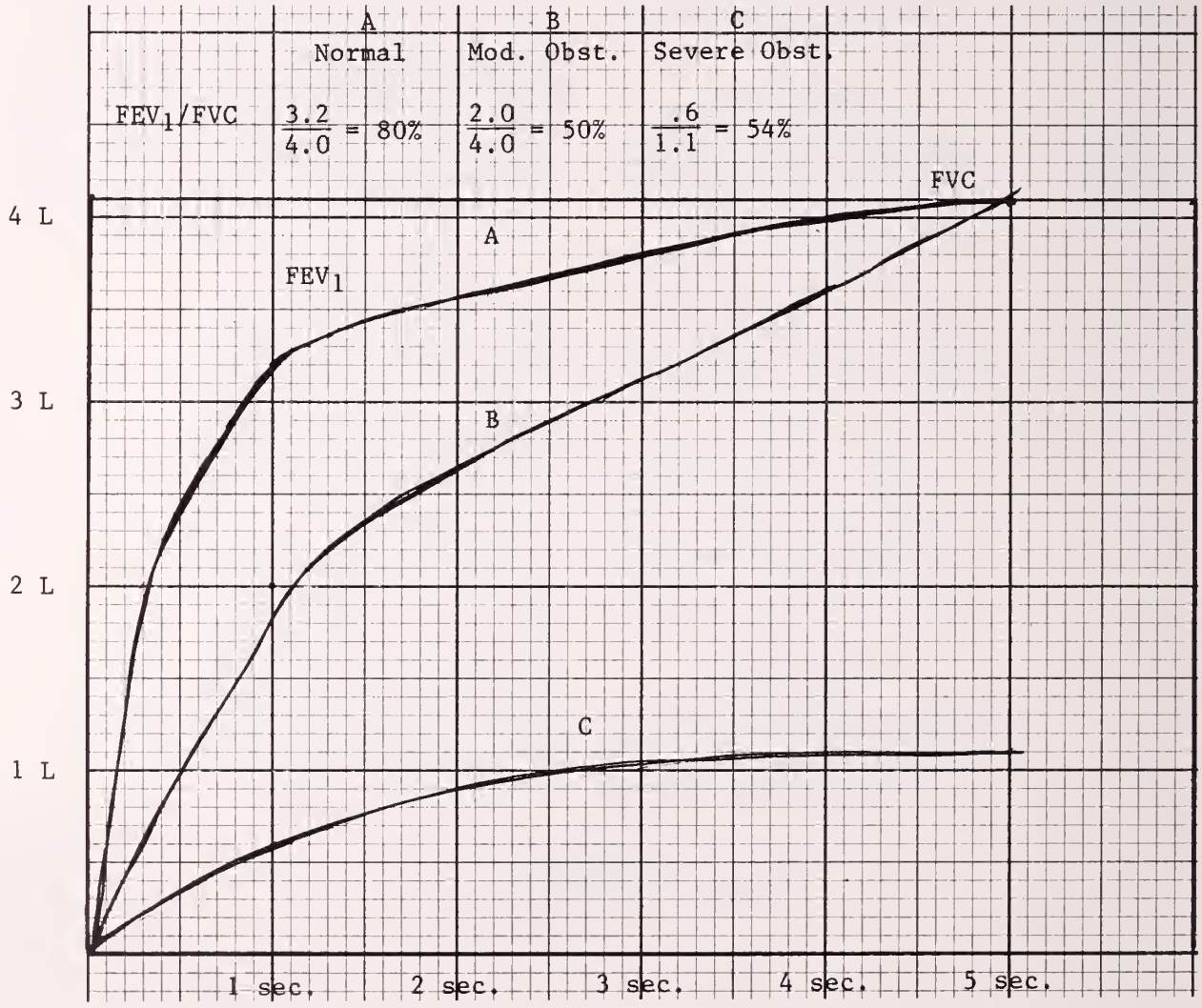

Figure 1. Expiratory Spirograms Demonstrating Curves For Normal Airways (A), Moderate Obstructive (B), and Severe Obstructive (C) Airway Disease.

wealth of information and it is so available.

Equipment and Personnel

To be interpretable the spirogram must be properly performed by the patient and technician. The technician should instruct the patient to first exhale completely, then inhale to maximum lung capacity and exhale completely as rapidly as possible on a forced vital capacity maneuver or exhale at a rate equal to that on relaxed exhalation on a slow vital capacity maneuver. If necessary, the patient should be encouraged by the technician to exhale completely during the expiratory maneuver. Three separate tracings of expiratory maneuvers should be obtained and the results of the best expiratory curve should be reported.

Table 1

Values of FEV_1/FVC Ratio With Customary Grading of Degree of Airway Obstruction

FEV_1/FVC	*Severity of Obstruction*
75-100%	Normal
60-75%	Mild
50-60%	Moderate
35-50%	Severe

The equipment used should be reliable and accurate. The bellows-type spirometers, such as the Vitalor® and Vitalograph,® and the water and waterless spirometers where the volume of air exhaled is translated directly onto a moving strip of paper are generally preferred. They have been tested for accuracy, reliability, ease of operation, durability. They are familiar to most physicians and they produce a written observable tracing of the patient's effort. Furthermore, this tracing can be repeated again and superimposed over the original tracing so that changes from one expiratory curve to another can be easily seen. These instruments, however, must be recalibrated and cleaned regularly to maintain accuracy.

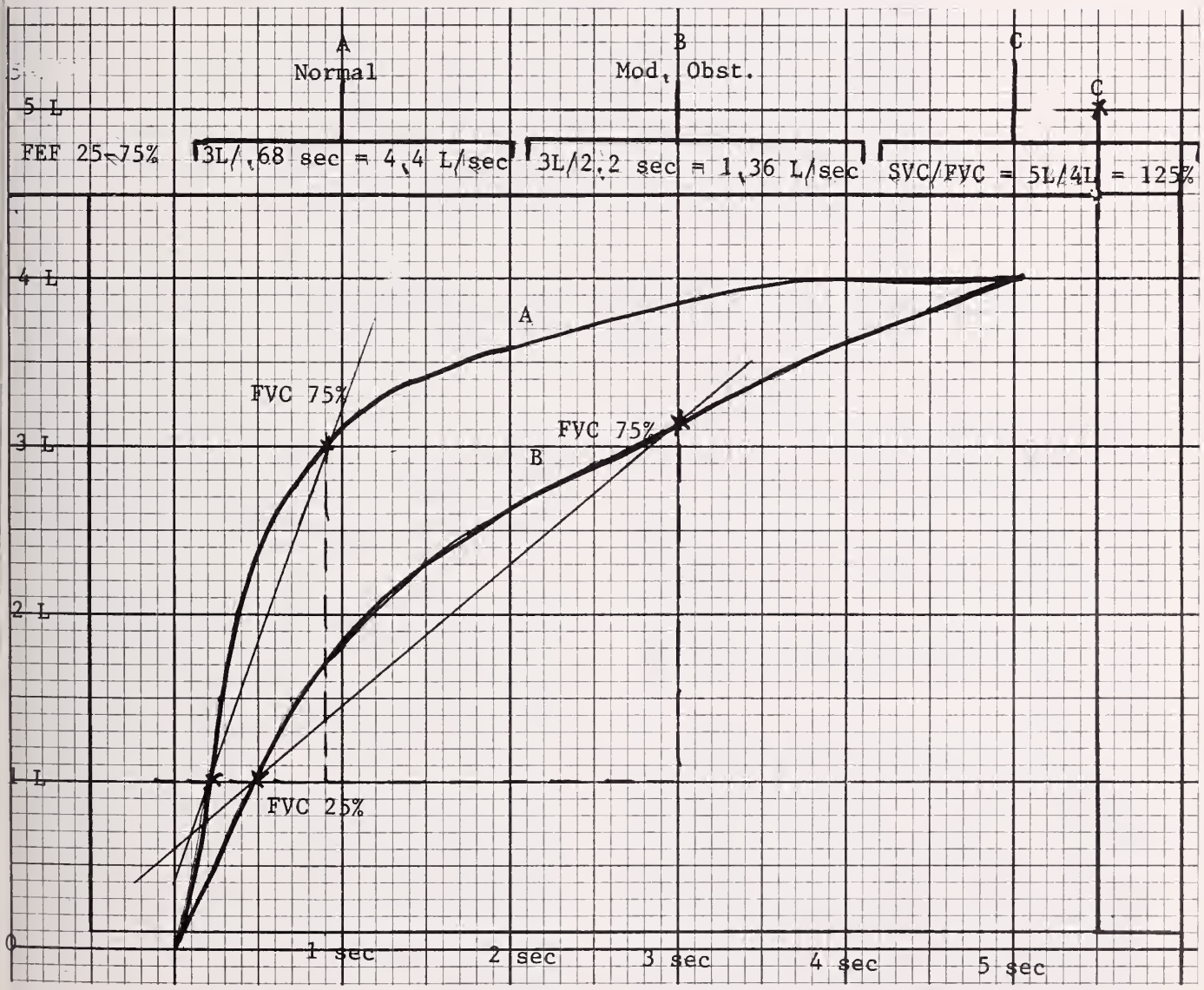

Figure 2. Expiratory Spirogram Demonstrating Measurement of FEF 25-75% on Normal (A) and Moderately Obstructive Curve (B). Ratio of SVC to FVC Demonstrating "dynamic air trapping" (C).

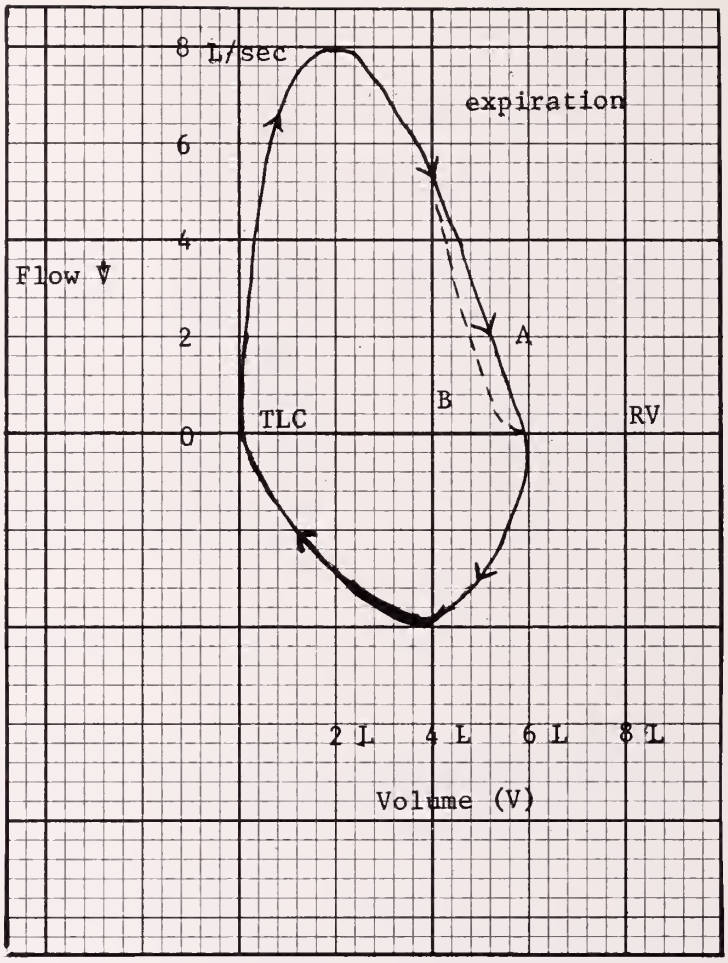

Figure 3. Normal Flow Volume Loop (A) and Flow Volume Loop Suggestive of Small Airways Disease with Typical "hockey stick" Appearance of Terminal Expiratory Flow Segment (B).

Recently, numerous electronic spirometers have been introduced which convert flow electronically into a volume signal which is reported as a numerical value. Some instruments have attachments that allow an expiratory curve to be produced on paper but these cannot be superimposed on each other. Initially these instruments were frequently inaccurate at high flow rates[1] but newer products appear to be accurate, reliable and easy to use although there has not been a controlled comparison of these electronic spirometers with bellows or water spirometers as yet.

Detection of Airway Obstruction

During breathing, the lung-thorax system acts as a bellows that provides fresh air to the alveoli for adequate gas exchange. Like springs, the lung tissue possesses the property of elasticity. When the inspiratory muscles contract, the thorax and lungs expand, and when the muscles relax and the force is removed, the thorax and lungs recoil to their resting position. Diseases of the lung tissue, such as emphysema, result in a decrease in elastic recoil due to a breakdown of alveolar septa and enlargement of lung spaces. The loss in elastic recoil results in excessively compliant or "floppy" lungs in which the airways collapse upon themselves more readily than normal on exhalation. This manifests itself as a reduction in maximal airflow during expiration or as an obstruction to airflow.

In addition to the elastic recoil forces, the respiratory muscles must overcome resistive forces in the airways during breathing. In diseases of the airways, such as in asthma and bronchitis, there is excessive airway resistance due to constriction of smooth muscle in bronchioles, edema in walls of airways and excessive secretions in the airways. This likewise results in decreased airflow or obstruction to airflow during expiration even with maximal effort. These conditions may be manifested clinically by the slowing of excursions of the chest wall during expirations.

Therefore, maximal expiratory flow is decreased in two types of diseases: 1) intraluminal disease of the airways, such as asthma and bronchitis; 2) disease associated with loss of lung "springs," such as emphysema.

The expiratory spirogram which records volume

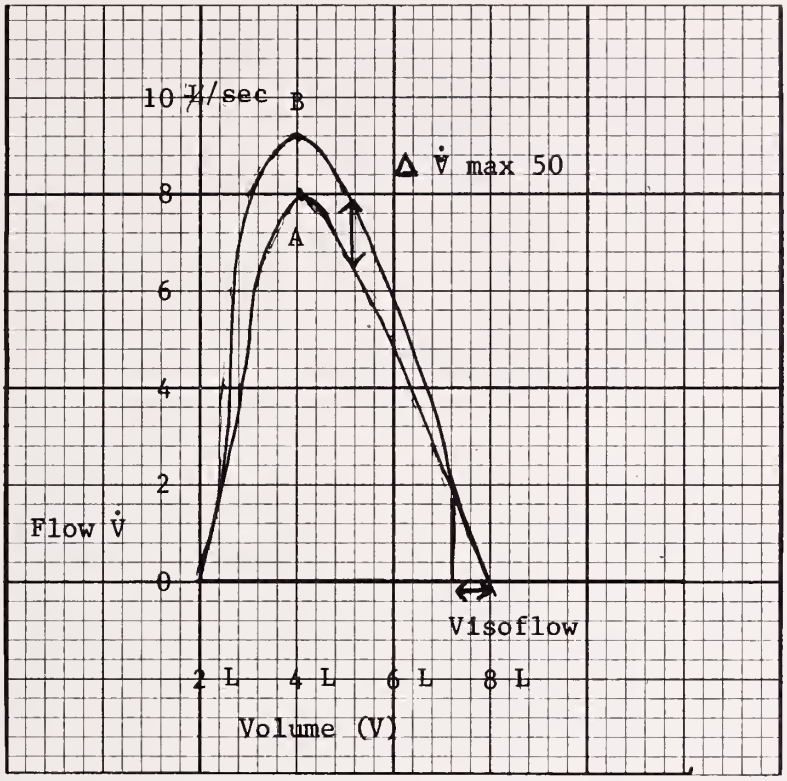

Figure 4. Flow Volume Loop performed by exhaling air (A) and repeated, exhaling a He-O_2 mixture (B). The change in expiratory flow at 50% of vital capacity (Δ V̇ max 50) and the volume at which the two curves meet (Visoflow) are indicated.

of air expired versus time, is used to confirm a decrease or obstruction in maximal expiratory flow. The classic expiratory spirogram of airway obstruction depicts a curve that represents a large decrease in the amount of air exhaled in the first second of expiration (FEV_1) but a near normal or normal total expired air volume (FVC) (Figure 1). Generally the ratio of the FEV_1/FVC indicates the severity of the airway obstruction (Table 1). Normally at least 75% of the total vital capacity should be exhaled in the first second. Anything less than 75% indicates some degree of airway obstruction.

As the degree of obstruction worsens, the total forced vital capacity or the total amount of air exhaled will decrease regardless of how long expiration is prolonged (Figure 1). In severe obstruction, the total vital capacity exhaled may be so reduced that the FEV_1/FVC ratio underestimates the degree of airway obstruction. In some cases, the FEV_1/FVC ratio may be almost normal or just within the normal range. This situation falsely represents a combination of obstructive and restrictive lung disease or just restrictive lung disease alone. Usually, the configuration of the curve with a slow linear increase in expired gas volume or examination of the patient will identify the severe obstructive defect. Occasionally, however, particularly in obese patients, the actual measurement of lung volumes will be necessary to make sure that a restrictive lung process is not present. In such cases, the absolute level of the FEV_1 is a more accurate predictor of the airway obstruction. Patients do not become dyspneic from their obstructive airway disease until the FEV_1 falls below 1.2-1.3 liters[2] but the greater the usual activity level, the sooner the sensation of dyspnea is reached. When the FEV_1 falls below .8 liters,[2] dyspnea usually occurs with very little activity such as shaving, eating, bathing, etc. If the degree of airway obstruction is followed serially, the FEV_1 can be expected to decrease by about .06 liters[2] per year simply as a consequence of aging. Decreases in the FEV_1 of more than .06 liters per year suggests ongoing active pulmonary disease of some type.

Frequently expiratory spirograms report the peak expiratory flow rate (PEFR) or peak expiratory flow between 25% and 75% of the vital capacity (FEF 25-75%). This value reflects the slope of the expiratory spirogram (Figure 2) and is obtained by drawing a line through the two points designated as representing 25% and 75% of the vital capacity respectively. This line is the slope of the spirogram and, by measuring its length and rise, a value for the FEF 25-75% in liters/minute is obtained. Decreases in the slope or slight flattening of the expiratory spirogram are postulated to represent very early or mild obstruction in the airways at a time when the other values (FVC, FEV_1 and FEV_1/FVC) are still normal. Because initial or peak flow rates are very effort dependent, these determinations are actually

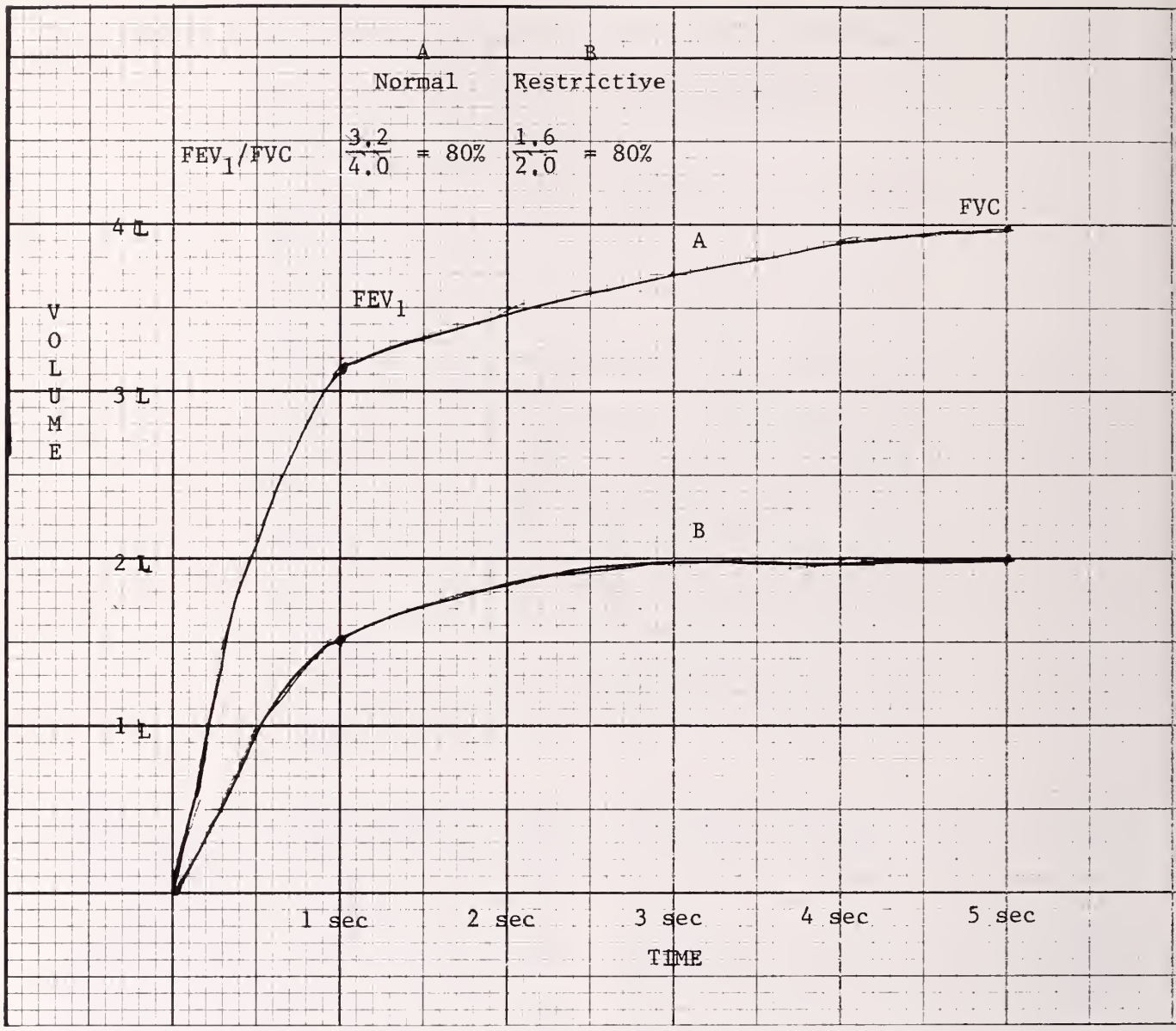

Figure 5. Normal Expiratory Spirogram (A) compared to Restrictive Curve (B) demonstrating decreased FEV_1, FVC but normal FEV_1/FVC ratio.

of limited value as there is much intra-individual and much inter-individual variation in the values obtained. Hence there is such a wide range of normal values that a true early abnormality is difficult to detect and a clearly abnormally low value indicates such severe obstruction that the FEV_1 and the FEV_1/FVC ratio are also abnormally low.

Whenever airway obstruction is detected on the expiratory spirogram, the study should be repeated after an inhaled bronchodilator. A 10% or greater improvement in the FEV_1 or FVC is considered a significant improvement. This type of study helps to predict who will respond to and how much they will respond to bronchodilator therapy. Frequently patients receive bronchodilator therapy despite the absence of any significant improvement in the expiratory spirogram. This is a rational and customary approach to therapy because the expiratory spirogram is not very sensitive at detecting small changes in airway function or in detecting obstruction in the small peripheral airways. In such instances, the patient's subjective indices of dyspnea are the best guideposts to judge the effectiveness of bronchodilator therapy in the absence of more sophisticated sensitive pulmonary function equipment. In summary, whether or not reversibility of airway obstruction is documented by spirometry, the patient's subjective response to therapy determines the course of further therapy.

More frequently in emphysema as opposed to other causes of airway obstruction, the amount of air exhaled is greater if exhalation is submaximal

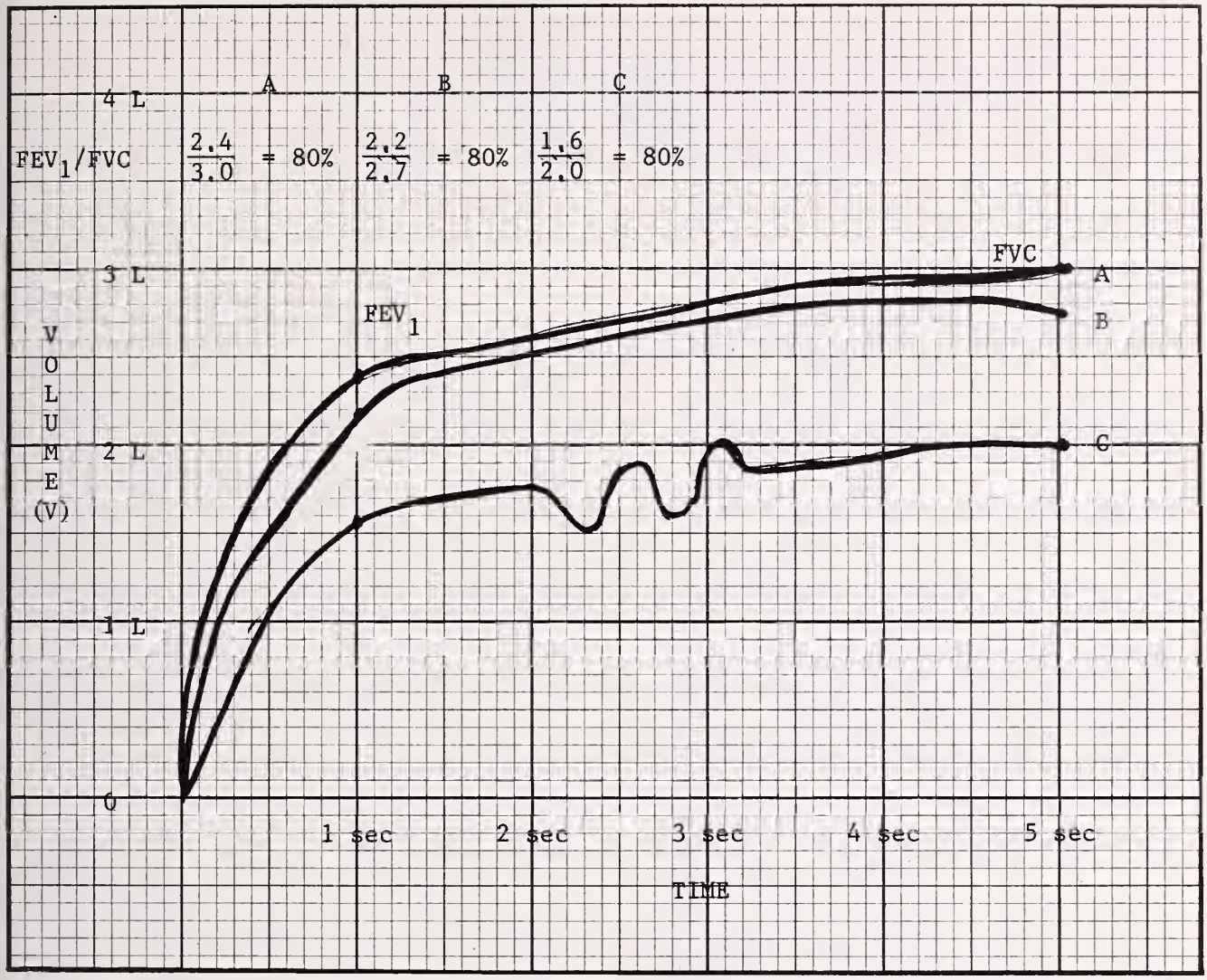

Figure 6. Three consecutive spirograms of an uncooperative patient demonstrating wide fluctuations between curves and a restrictive defect with decreased FEV_1, FVC but normal FEV_1/FVC ratio on each curve.

and prolonged (slow vital capacity). Due to the loss of elastic recoil in emphysema the airways tend to collapse sooner if expiration is performed with a maximal effort. This results in a slow vital capacity volume which may be considerably larger than the forced vital capacity volume. This is referred to as "dynamic air trapping" and it is defined as an SVC/FVC ratio of greater than 110% (Figure 2). It indicates that some if not all the airway obstruction is due to emphysema.

Finally, with so much information able to be gleaned from an expiratory spirogram, it is well to acknowledge its limitations. While the study is simple and inexpensive, it is insensitive to mild changes in airway function particularly in the small airways of less than 2 mm. in diameter. In normal lungs, 80-90% of the total resistance to airflow resides in the large or medium size airways larger than 2 mm. in diameter.[3] Changes in the dimensions of these airways, such as due to bronchospasm, may be detected by the expiratory spirogram. The expiratory spirogram is of little use in the early diagnosis of disease in smaller airways of less than 2 mm. in diameter. This is because the total cross sectional area of these small airways is large and their resistance to airflow is a small component of the total airway resistance (10-20%).[4] Consequently, there may be a considerable narrowing of these airways before a change in the expiratory spirogram occurs. Therefore, evaluation of obstructive disease in these small airways which has been shown to occur as a result of cigarette smoking[5] requires other pulmonary function tests. A qualitative assessment of obstruction in these small airways can be seen by observing the terminal portion of the flow-volume loop which represents airflow in these airways (Figure 3). A quantitative assessment of obstruction in the small airways can be gained by performing any of a number of pulmonary function studies[5] but the current study in vogue is the measurement of the volume of isoflow (Viso) and the change in flow rates at 50% of vital capacity ($\Delta \dot{V}$ max 50) by comparing a

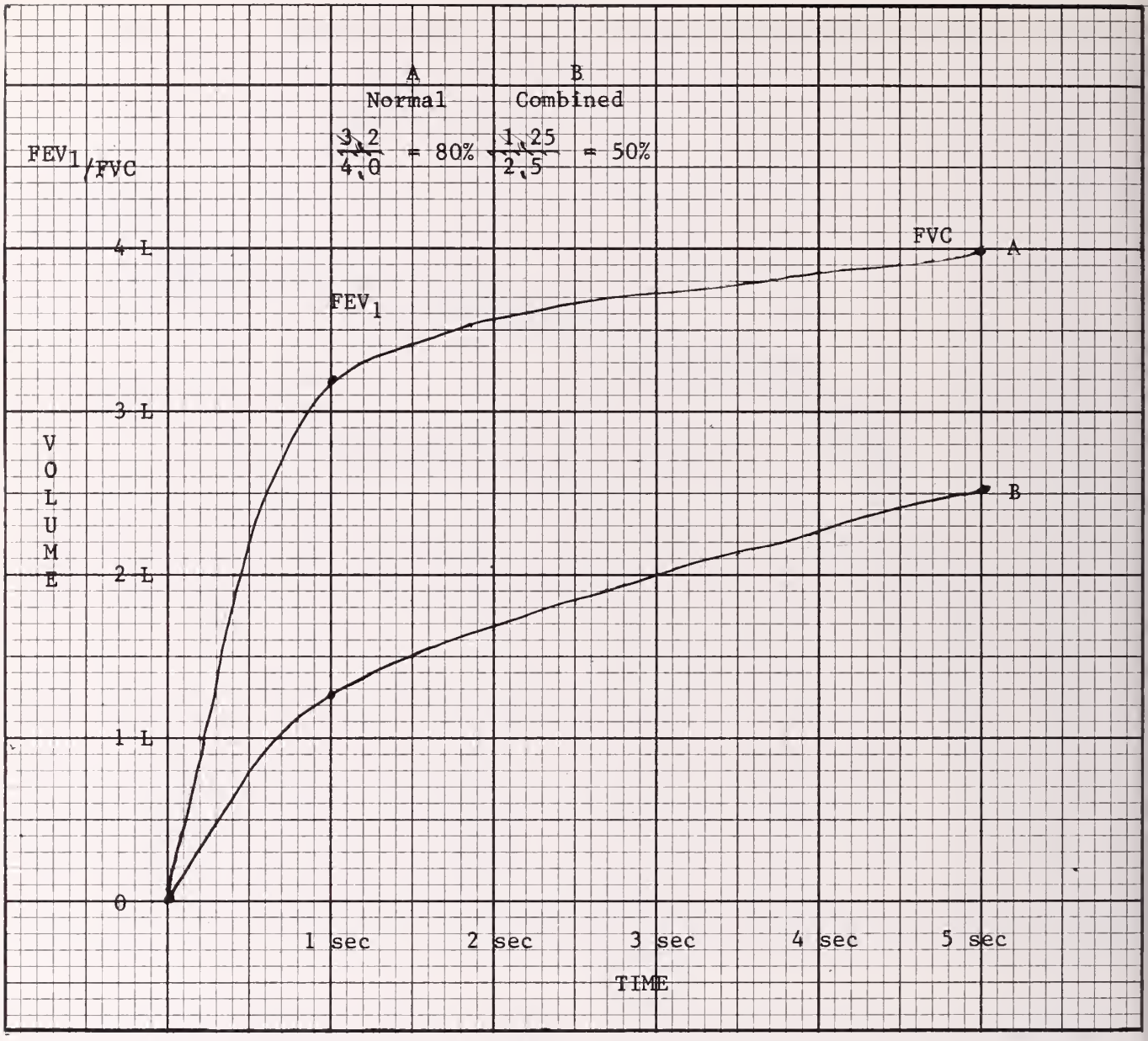

Figure 7. Normal Expiratory Spirogram (A) compared to another Spirogram demonstrating a mixed or combined obstructive and restrictive defect with a decreased FVC, greatly decreased FEV_1 and decreased FEV_1/FVC ratio (B).

flow volume loop performed by exhaling air and then performed by exhaling a mixture of 80% helium and 20% oxygen[6] (Figure 4).

In summary, the expiratory spirogram is useful in the detection and quantitation of obstructive lung disease, in the serial longitudinal evaluation of the disease and in the response to treatment of such diseases. Examples of obstructive lung disease are emphysema, bronchitis, asthma, cystic fibrosis and bronchiectasis.

Detection of Restrictive Diseases

Diseases of the lung, such as pulmonary fibrosis and pneumonia, interfere with the elastic behavior of the lungs and make them "stiff." Patients with "stiff lungs" generally have decreased or restricted lung volumes. The expiratory spirogram will confirm the restricted lung volumes by inscribing a curve that is proportional but smaller than normal. The characteristic finding is the decrease in the forced vital capacity (FVC) with a proportionate decrease in the FEV_1 such that the FEV_1/FVC ratio remains normal. A normal vital capacity rules out significant restrictive lung disease (Figure 5).

Many other conditions other than "stiff lungs" will result in a restrictive defect on the expiratory spirogram. These include poor-patient cooperation, muscle weakness, chest deformity such as kyphoscoliosis, previous resection of lung tissue and disease in the pleural space. Of these possibilities, poor patient effort is probably the most frequent cause for a restrictive defect on the spirogram. This can be

detected by observing the actual spirogram tracings which will usually show wide variation in maximal airflow on each tracing (Figure 6). Checking the FEV_1 against the MVV (maximum ventilating volume) is another internal check to detect poor patient effort. Usually 40 x FEV_1 will closely equal the MVV. The uncooperative patient will generally have an MVV which is below that expected based on the FEV_1 x 40. Muscle weakness, however, will exactly simulate poor patient effort on the spirogram and must be distinguished by clinical observation.

If suspected on the spirogram, it is advisable to correlate the spirometric findings with actual measurements of the total lung volume and its various subdivisions. Measuring lung volumes will more conclusively document the presence of a restrictive process and will accurately document the severity or extent of the restrictive process. With a restrictive process, the total lung volume (TLC) must be decreased and each subdivision of the total lung volume will be proportionately decreased. In chest wall disease, however, such as kyphoscoliosis which prevents the small lungs from emptying, the vital capacity is severely restricted and the residual volume (RV) is normal or near normal such that the RV/TLC ratio is elevated as is seen in the hyperinflation of RV in obstructive airway disease.

Combined Obstructive and Restrictive Defects

In addition to the possible combination of a disease causing airway obstruction with a disease causing restrictive lung disease, congestive heart failure, extrinsic allergic alveolitis and sarcoidosis may cause a combined obstructive and restrictive defect. This combined defect can be suspected on spirometry but should always be confirmed by measurement of lung volumes. The spirometric tracing will show a large decrease in the forced vital capacity, a moderate decrease in the FEV_1 and a mild decrease in the FEV_1/FVC ratio (Figure 7).

Conclusion

The "screening" expiratory spirogram, therefore, provides a wealth of information by establishing the presence of abnormalities in the airways, alveoli and thorax. This test is useful in:

1) the differential diagnosis of all patients with dyspnea,
2) the evaluation of patients before intrathoracic or extrathoracic surgical procedures,
3) the determination of the risk of using certain diagnostic procedures,
4) the detection of early respiratory failure and the monitoring of procedures in a respiratory or intensive care unit,
5) the quantitative evaluation of specific therapeutic procedures in a patient already known to have bronchopulmonary disease, and
6) the epidemiologic studies of populations to provide clues to the causes of pulmonary disease.[7]

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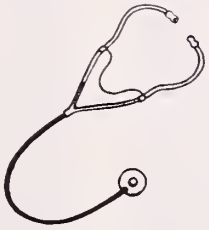

Rehabilitation at Mid-Maine Medical Center

The Team Approach

J. S. DIGGS, M.D.*

Almost everyone agrees that rehabilitation is an important part of medical/surgical care. The word has become a common term in federal and state legislation. Deciding what it means and providing implementation is not always easy on the practical level of a community hospital. The following article is a description of the effort at Mid-Maine Medical Center to develop a new program.

Three years ago the Center decided to add a full service Department of Rehabilitation Medicine to its efforts in Alcohol and Psychiatric Rehabilitation. I was hired in October 1976 as the first full-time Physiatrist. A separate 14-bed service has been established at the Seton Unit with the following support: Physical Therapy, Occupational Therapy, Social Services, Home Health Agency, Clinical Psychology, and the F. T. Hill Speech and Hearing Center. Care is coordinated with out-patient services, the amputee clinic, arthritis clinic, and pediatric clinics. At the request of Sebasticook Valley Hospital and Camden Community Hospital, rehabilitation services are shared by establishing a regular monthly consultation service. Physical Therapy sends one therapist to Pittsfield on a part-time basis, and the Hill Center has helped develop a new speech and hearing program in Camden and Augusta.

Justification for 14 Rehabilitation Beds: A separate bed unit and nursing service was established following the rule-of-thumb that a community hospital will have a need for rehabilitation services for 3% to 5% of its total number of beds; in our case 337 beds. Difficult cases involving multiple or severe injury can be properly handled only with a team approach with all the members listed above available on a full or part-time basis.

A common mistake made by both physicians and administrators in any size hospital is to think that a physical therapy department is a rehabilitation department. In the isolated case of an orthopedic musculoskeletal problem, physical therapy may be the only rehabilitation effort added to the medical/surgical threatment, but for the multi-trauma patient, stroke and especially spinal cord injury, the physical therapist is a member of the team. A physician, nurse, and physical therapist can go a long way in treatment of many problems, however, the same physician, nurse, and physical therapist must also know when a problem requires what is now accepted and defined as a holistic team approach which can only be provided in a team rehabilitation setting.

With or without a rehabilitation department, a rule-of-thumb percent can also be applied to physical therapy. A hospital can expect 10% to 15% of its total inpatient population to require some effort from physical therapy. This may range from crutch walking instruction to the more complicated, progressive training involved with a postoperative orthopedic case. Successful maximum utilization depends on good response to the needs of the patient and the referring physician. This depends on availability, quality of care and communication. The above percent of inpatient utilization should be doubled by the outpatient caseload. Economically, the gross physical therapy department income should be double the overhead.

Hospitals must give special attention to the establishment of a rehabilitation program in a community hospital because the acute care setting precludes attention to the details of caring for patients with chronic diseases. The rehabilitation team must focus on the goal of maximum independence for the patient by stimulating the patient to perform for himself a maximum number of services. This is not compatible with a physician and nursing staff where patients are acutely ill and services must be provided for them. Financial and administrative support and understanding are necessary to establish the team approach which requires expensive initial outlay of space, personnel, and equipment.

Team Effort For In-Patient Rehabilitation: Treatment is based on the problem list which reflects all the needs of an individual case. When treatment is given by more than two people (physician and nurse), there must be regular team communication. At Mid-Maine Medical Center, a weekly rehabilitation meeting is held to go over each new case and to re-evaluate all other patients on the service — problems, goals and effective utilization take place at the same time. Ward rounds are made Monday morning to start the week, and Thursday morning rounds facilitate discharge plans or activities and exercises the nurses can continue doing for patients over the weekend. Patients expect different service from different members of the program. As soon as a patient makes progress in physical therapy or occupational therapy, the word must get to nursing who will then know to support continued independence rather than allowing a patient to go back to a "sick" role and manipulate the nursing service to promote dependence for feeding, dressing, standing, transfers, exercise, and activities of daily living.

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The basic approach of rehabilitation is *prevention*. Bed sores, contractures, muscle atrophy, urinary tract infections, and psychological depression are all preventible complications of chronic illness. Decubitus ulcers can only be prevented by proper nursing attention. The development of skin pressure sores is an obvious and direct measure of the level of nursing care. The best articles for prevention of skin sores are found in nursing books and journals. Prevention of skin sores should be as automatic as bathing and range of motion to prevent joint contracture. Physical therapy and occupational therapy can be of assistance to start a range of motion program but on a daily basis it is the nurses who can best guide the immobilized part through a full range of motion. Nurses must also teach aids or family members to take over this routine job as part of discharge planning. Urinary tract infections can usually be prevented by following established and proven techniques of care that are unfortunately not widely practiced. Psychological depression which is reflected in the staff, relatives and other visitors, usually is corrected when an active, disciplined treatment program is initiated.

A successful team must include a variety of allied medical professionals listed in the second paragraph. The physician must learn to participate effectively in a team process and listen to any member who has something to contribute. Only when physicians can treat these persons as professional colleagues whose judgement and skill can be trusted will they be able to contribute what they should to the rehabilitation program.

Rehabilitation Nursing is the foundation of any program. The other therapists cannot begin their efforts until the nurse has controlled the problems of bowel, bladder, skin, food, and fluid intake. It is difficult for the patient and a therapist when bowel incontinence occurs during exercise on a physical therapy mat. Time and money are wasted until the bodily funcitions are controlled by the nursing program which ideally is started on the day of admission.

A rehabilitation nursing service should be free to direct the daily program without awaiting detailed instruction. It is a mistake for the physician in charge not to delegate adequate responsibility to the nurses once they are trained and competent in the special aspects of chronic care rehabilitation techniques. The physician can expect the nurse to call to his attention the problems that come up relating to control and prevention of trouble with bowel, bladder, skin and food, fluid intake. If the nurse assumes the responsibility of controlling the patient's time, the physician does not need to become involved in minutia. There is no question regarding the patient's care, but the supervisor is free to use her professional judgement and assume the direction of her staff.

Nursing care plans and responsibly should be written in a notebook and kept on the station as standing orders or under a general heading of "treatment plan" to cover the basic care of bowel, bladder, skin, and fluid/food intake. Nurses carry out the activities learned in physical therapy and occupational therapy, coordinate the activity schedule, provide a setting as close to the home situation as possible, and make arrangements for easy transition to home and maintenance care.

The Physical Therapist is used to evaluate level of physical function, give therapeutic exercises, and direct progressive training. They are most effective in evaluating each patient by performing specific tests; planning a treatment program as a result of the evaluation and presenting the program to the physician for approval, carrying out the program in coordination with weekly team conferences under physician supervision; instructing non-professional workers and relatives in carrying out the specific procedures and supervising their work; instructing community health agencies in following a patient's maintenance program at home.

The physician should give therapists only general directions regarding patient care. Detailed treatment prescriptions given to therapist, nurses or other specialists, waste the physicians time and limit the potential contribution of highly trained, well qualified specialists.

An Occupational Therapist is a specialized therapist who works to improve the functional aspects of the handicapped and the activities of daily living. Unfortunately, many physicians do not know how to use this department and by history they are too often thought of as providing diversion. A special contribution is their skill in making adaptive equipment including splints and helping a patient to develop maximum use of the extremities for self care and sometimes an occupation.

The occupational therapist, as in physical therapy and nursing, treats for prevention of deformity and physical restoration of the patient with special attention for the maximal level of independence in self-care with exploration of occupational and avocational potential. The occupational therapist will measure and objectively evaluate the patient's physical and psychological condition including: range of motion, strength, motor dysfunction, sensation and perceptual-motor dysfunction. During this process, the therapist must assess the level of patient understanding and observe what he considers his needs to be. As a member of the rehabilitation team, the therapist must combine the findings with the patient's diagnosis and the findings of all other members of the team at the weekly conference or on a daily basis when there is rapid progressive improvement. When a patient's function can be enhanced with adaptive equipment, the occupational therapist works to design custom made devices ranging from eating utensils to complex hand splints or arm devices.

Nursing, physical therapy and occupational

Continued on Page 46

Random Thoughts

EDWARD G. MEHRHOF, M.D.*

When I moved to Maine in July 1977, I found myself wondering what differences and what similarities I would find in the people of the State who became patients, in the treatment facilities, and in the professional staff. After about four months of working at Mid-Maine Medical Center and the Augusta Mental Health Institute, I can't find too many differences from what I was used to in Kansas. There are a few exceptions. I have been told that the relatively sparse population results in a degree of isolation which manifests itself in both independence and depression and also in some resistance to other people's point of view. I have also been told that the long winter leads to a greater incidence of intra-family violence. The winter need not result in violence because there are so many things to do in the winter such as skiing, skating, sliding, snowmobiling, etc. Probably the lack of money keeps people from enjoying this time of year.

I've noticed that there is a great deal more reliance on psychotrophic drugs than I've been used to. In Topeka we were taught that the main treatment is psychotherapy and drugs were used to facilitate the talking therapies. Also, I've noticed that the courts tend to think of psychosis as the only type of mental illness and that the neuroses and character disorders are not classified as mental illness. I remember having to convince a few members of the staff at the Augusta Mental Health Institute that both neurotic patients and those with characterological problems may require hospitalization.

I really want to write a few words about an area of our psychic life that psychiatry in both Kansas and Maine and in fact all over has neglected — that area is *happiness*. Happiness is an emotion that feels good to experience and feels not so good to not experience. A larger question for psychiatry is how to conduct our lives such that we will experience as much happiness as we can. I realize that some people find happiness in negative acts but for the moment I am not thinking about them. The best book on this subject that I have read is *Positive Addiction* by William Glasser, M.D. In general, Dr. Glasser states that happiness can be experienced through *loving* and doing things that the individual feels are *worthwhile*. In order to have the psychic strength to do things that are worthwhile, the individual should become addicted to a positive activity such as running, swimming, rowing, bicycling, cross-country skiing, etc. To become addicted we need to do the activity for about one hour a day, seven days a week. It takes 3-6 months of progressive activity to attain the addiction.

The first part of Dr. Glasser's prescription for feeling happy is loving. Anyone who has been in love knows that this is about the most pleasant feeling there is. Although he does not go into this aspect too much, I believe he is referring to romantic loving and not the love parents have for their children or for their friends or for their own parents. This does not negate these latter types.

A second area of psychic life that I feel has been neglected by psychiatrists is religion. It is hard to not be impressed by the radiant faces of those we see that are fully committed to their religion. When I have watched, I've seen this very often with people participating in the revival or evangelistic ministries. I've also seen this with people in church. Belief in a higher power or a spirit of goodnees helps a person get out of his own "skull" for a period and become captivated with something more important and uplifting.

In regard to doing things that we feel are worthwhile, I think this is easy to test out many times per day. I think all of us feel good or happy with ourselves when we are doing something positive, thoughtful and results in benefit for someone.

These are just some random thoughts that I believe are true and valuable.

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REHABILITATION AT MID-MAINE MEDICAL CENTER: The Team Approach

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therapy help patients reach their maximum physical potential in their previous environments or in new environments more suited to their altered capabilities. Detailed prescriptions are not needed and would actually be harmful for the physician to give. The patient's needs are translated into a problem list which leads to the goals and treatment plan which is then followed by the team working to find solutions.

Over the past year Mid-Maine Medical Center has been able to establish the basic program described. In addition to the satisfaction of working in such a cooperative setting, I am fortunate to be able to assist in the development of new programs at Sebasticook Valley Hospital and Camden Community Hospital.

Dopamine Induced Gangrene

ROBERT NOGLER* and MARTIN KEIBEL, M.D.**

A patient with severe and prolonged cardiogenic shock following myocardial infarction recovered after treatment with large amounts of dopamine. Pedal gangrene, a recently recognized effect of large doses of dopamine, complicated the patient's recovery. This case report reviews the literature and discusses prevention and treatment of dopamine induced gangrene.

CASE REPORT

A previously healthy 71-year-old man was hospitalized because of retrosternal chest pain. Except for sweating, examination revealed no abnormalities. Vital signs were normal. Peripheral pulses were adequate. EKGs and serial cardiac enzymes established the diagnosis of posterior myocardial infarction.

The second day the patient became confused. Blood pressure and urinary output fell to shock levels. Chest film revealed significant vascular congestion. Cardiac shock continued with systolic blood pressure < 80 mm Hg and urine output < 20 ml/hr.

Initial therapeutic measures included fluid challenge and nasal oxygen. Later, a dopamine drip was begun at the rate of 20 micrograms/kilo/minute. Moderate control of the heart failure was brought about using a regime of dopamine 50-60 mg/kg/minute, furosemide, lidocaine and intubation with respirator assisted respiration.

Although the urinary output and blood pressure were maintained by dopamine and other treatment, the patient became stuporous.

Definite improvement was first noted by the 8th day when the patient was extubated. The patient continued to require large amounts of dopamine; on the 9th day his toes became cyanotic. Attempts to decrease the dopamine precipitated drastic falls of blood pressure and urinary output. Other measures did not sustain the vital processes so the dopamine drip was continued and the toe cyanosis progressed. From the 12th day, progressive improvement occurred despite other complications including bacteremia, gastrointestinal hemorrhage and atrial arrythmias. At discharge on the 32nd day, the patient seemed completely recovered mentally and physically except that his toe lesions had progressed to "dry" gangrene.

DISCUSSION

Treatment of cardiogenic shock is directed to correction of hypovolemia, anoxia, acidosis and pump failure. Vasoactive amines that stimulate heart muscle contraction are part of the therapeutic effort and have been used with varying degrees of enthusiasm. There is general agreement that norepinephrine and dopamine are the most useful of the vasopressors. Although dopamine is an immediate precursor of norepinephrine and in chemical structure lacks only a hydroxyl group on the side change, dopamine produces an unusual type of vasodilation in various vascular beds in addition to stimulating myocardial contraction. Vasodilation occurs in renal, mesenteric, coronary and cerebral vascular beds. Dopamine also regularly produces vasoconstriction of arteries and veins in all areas when large doses are used. Goldberg[1] has summarized evidence suggesting that dopamine reacts with specific dopamine receptors to produce its diverse effects.

Adverse effects of dopamine are generally considered to be ventricular dysrhythmias, angina pectoris and nausea and vomiting. With increasing use, dopamine associated gangrene has been recognized although multiple factors might be involved — severe hypotension, disseminated intravascular coagulation and pre-existing vascular disease as well as dopamine. Alexander[2] reported pedal vasoconstriction that progressed to gangrene despite discontinuation of the dopamine. In his report, Alexander also described three patients who developed cyanosis and gangrene in the fingers following the use of dopamine after mitral valve replacement and in treating frostbite. In one instance in which dopamine had infiltrated the skin, gangrene apparently was averted by administration of phentolamine. One comment on Alexander's report cited the failure of sodium nitroprusside to reverse vasoconstriction complicating dopamine,[3] but in another instance apparent control of cyanosis and prevention of gangrene was effected by intermittent use of chlorpromazine.[4] Possibly the best way to prevent peripheral constriction induced gangrene would be to add alpha adrenergic blocking agents such as phentolamine and phenoxybenzamine to dopamine when dopamine is used for treatment of shock and certainly when dopamine is used in large doses.[1]

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Electronystagmography

LORING W. PRATT, M.D., F.A.C.S.* and ANNE L. GIROUX, Sc.M.**

The evaluation of the dizzy patient is one of the most exacting problems encountered in medicine. Because of the many diseases and conditions which produce dizziness and the several systems involved in its production, it is often desirable to make a multidisciplinary approach to the evaluation of the patient with dizziness. Because of the serious potential of this symptom, careful investigation is essential.

The first and most important evaluation is that of the general medical and physical condition, in an effort to determine the presence or absence of systemic disease such as hypertension, diabetes and other systemic disorders.

Then specialized examination, such as examination of the ears, should be performed to determine the presence or absence of diseases such as nonsuppurative otitis media, otitis media purulent acute, otitis media chronic, the presence of labyrinthine fistulae, and in addition, physiologic testing of the internal ear to obtain information about both the cochlea and the labyrinth. Because the anatomical relations between the cochlea and the labyrinth are so close and they are so intimately interrelated functionally, both end organs must be studied. The perilymph in which the membranous labyrinth floats is common to both cochlea and vestibule, and the endolymphatic fluids which are contained in them are also common to both systems. Because of this close connection, careful evaluation of the cochlear part of the labyrinth is the first and most important study to make. This may be accomplished by audiometric studies which give reliable, objective data about the normal physiologic health of this organ and also its pathologic state.

Objective evaluation of the vestibular division of the internal ear is a complicated and difficult procedure because of the complex neurological pathways which connect the vestibule, the central nervous system and the extraocular muscles. Because of the vital importance of its function to the individual, only noninvasive reversible experiments upon this system have proven practical.

Historically, a number of tests have been used to evaluate the function of this system. For example, the Baranay Chair, or the torsion swing is used to stimulate the semicircular canals by rotation, which in turn stimulates the labyrinth. These rotation tests have one inherent problem in common. They stimulate both ears simultaneously. It is impossible by rotation tests, to separate the function of one ear from the other.

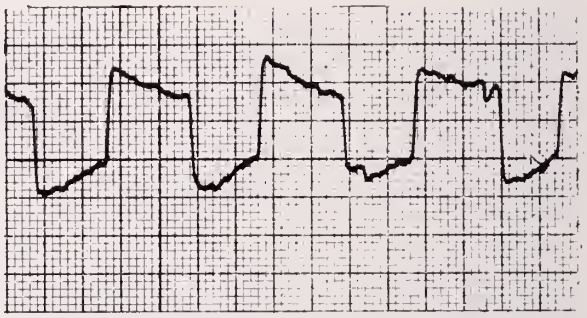

Figure 1. Example of a normal saccade Test.

The use of caloric stimulation permits the evaluation of one ear without interference from the other ear. The most common test is dependent upon the use of ice water as a stimulus. One cubic centimeter of ice water instilled in the external ear is the test designed by Kobrack, in which the labyrinth is stimulated by extraction of heat from the middle ear by ice water introduced into the external auditory canal. This sets up convection currents within the labyrinth and in turn produces a violent stimulation to the labyrinth. This test evaluates a single ear, but has the disadvantage that it is a maximal stimulus and has been likened to testing hearing with a pistol shot. This is a maximum stimulus and does not indicate the effect of stimulation at or near threshold level.

It is most logical to stimulate the ear at threshold level and to utilize an objective method of recording the results. With the Kobrack test, visual observation of the eye movements is used to determine and record the type of nystagmus produced. Timing the duration of the nystagmus has been the standard method of recording the duration.

Electronystagmography includes the use of a minimal stimulus. Irrigation of the ear canal with both cool and warm water, used alternately, is the stimulus, allowing a period of time for recovery between tests. The use of either cool or warm air is practical in the case of a perforated tympanic membrane. The electroencephalographic type recorder, by transducing changes in electrical activity arising in the extraocular muscles, provides a written record on a moving strip of calibrated paper.

The technique of testing is simple. The unmedicated patient (any anti-vertigo, tranquilizing or alcoholic medication must be terminated at least 24 to 48 hours prior to the time of the test in order to provide the patient with potentially good response to the test) can be tested with a variety of visual and vestibular stimulations.

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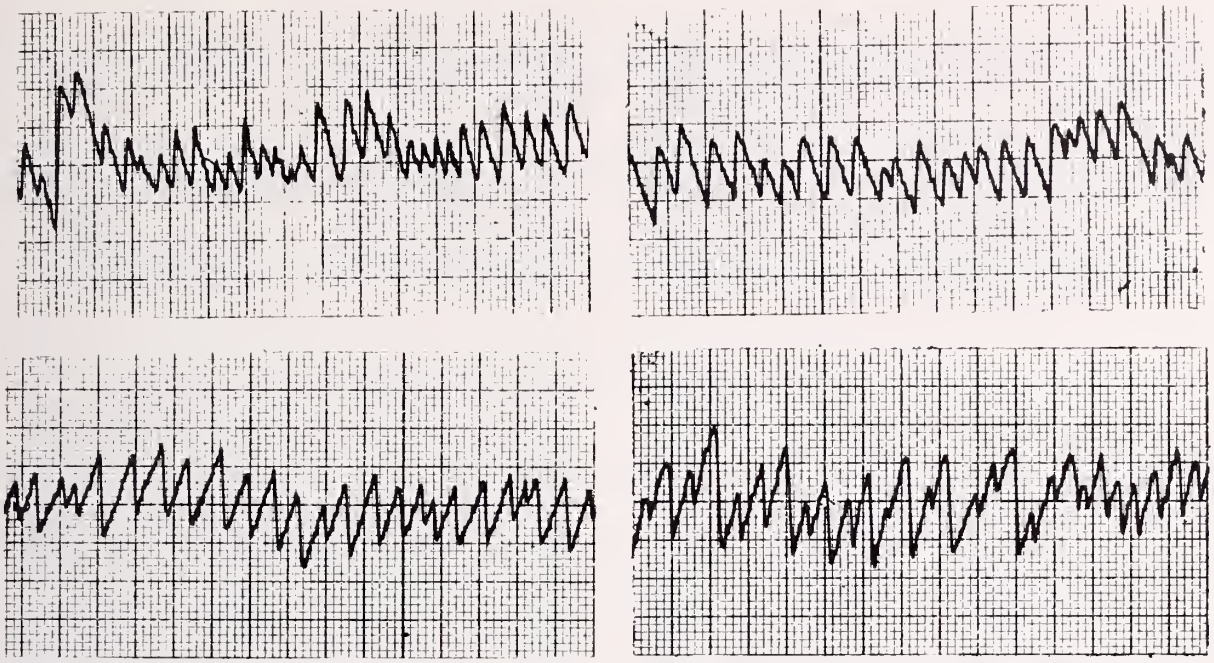

Figure 2. Example of normal optokinetic responses. Upper left: right to left — slow. Upper right: right to left — fast. Lower left: left to right — slow. Lower right: left to right — fast.

The amplitude calibration is determined in relation to the deviation of the eyes for a standard calibration angle of twenty degrees when looking to left to right, or up and down. This calibration factor relates the eye motion to the amount of pen deflection, and from these data quantitative evaluation of the amount of deflection of eye movement may be made.

The patient is stimulated by positional changes in order to determine the effect of head position and head motion upon the production of nystagmus. Eye movements are studied when tracking an object, such as that produced by optokinetic stimulation, or of pursuit task in following a target in sinusoidal movement.

After these visual and motion tests have been completed and the positional tests have established the basic function of the labyrinth, further studies are made. Cool water and warm water are utilized as stimuli in each ear separately, and the nystagmus thus produced is recorded by the electronystagmograph. Data are obtained and recorded for future study to help locate the site of lesion.

The tests routinely performed by technicians and interpreted by physicians are:

1. Saccade Test. Ocular dysmetria is determined by the overshoot or undershoot of ocular rotation that occurs when visual fixation is transferred from one place to another. This ability can be determined from the recorded amplitude calibration portion of the test. Fifty percent of the calibrations must include overshoots to indicate either cerebellar or brainstem pathology (Fig. 1).

2. Gaze Test. This test examines the eyes for nystagmus, and paresis of ocular deviation. Gaze is maintained for thirty seconds at fixation points of 20 and 30 degrees to the right, left, above and below center. The presence of gaze nystagmus or ocular paresis is indicative of central nervous system pathology. The normal test shows no nystagmus.

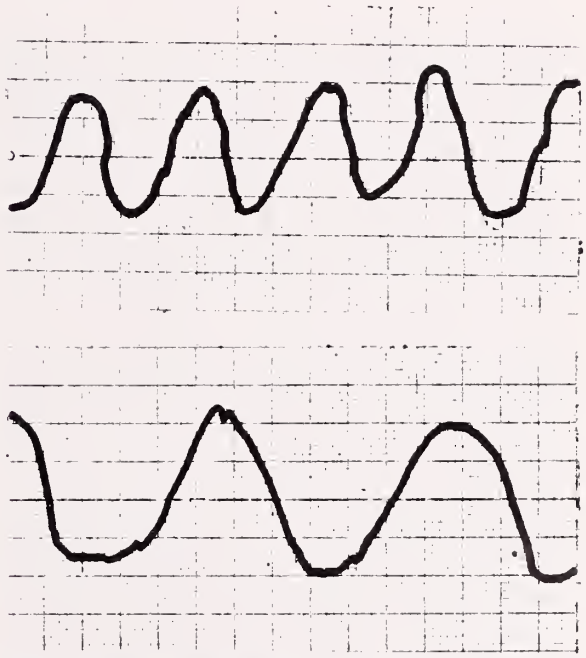

Figure 3. Example of a normal pursuit of a sinusoid: Top — fast: Bottom — slow.

3. Spontaneous Nystagmus. Recording of spontaneous nystagmus is done with the head in an upright neutral position with the eyes open as well as with the eyes closed. The presence of spontaneous nystagmus can result from vestibular, ocular or central pathology.

4. Optokinetic Responses. Nystagmus is nor-

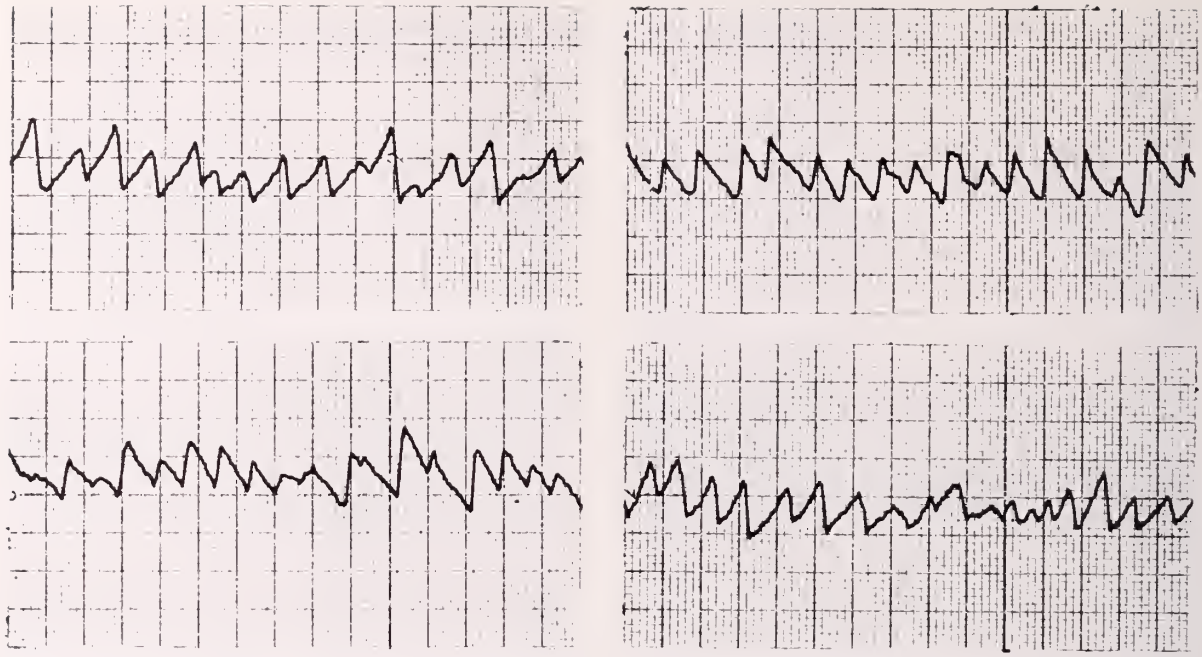

Figure 4. Example of nystagmus produced in a normal ear by 30°C and 44°C. Upper left: Right ear 30°C stimulus. Upper right: Left ear 30°C stimulus. Lower left: Right ear 44°C stimulus. Lower right: Left ear 44°C stimulus.

mally produced by looking at a moving repetitive pattern for both slow and fast speeds. Abnormalities with the horizontal stimuli indicate central oculomotor pathology. Vertical stimulus anomalies indicate a lesion high in the midbrain (Fig. 2).

5. Tracking Test. Fixation on a point in a moving sinusoidal pattern results in a smooth tracing of the sinusoid. Poor pursuit movement suggests central oculo-motor (brainstem) lesions (Fig. 3).

6. Dix Hallpike Maneuver. A rapid movement from a sitting to a head-hanging and turned position elicits paroxysmal nystagmus toward the pathological ear. A positive test suggests a peripheral lesion when unilateral. Bilateral response suggests either a peripheral or a central nervous system lesion.

7. Positional Nystagmus. After testing in the standard head positions, the tracings are examined for direction-changing or direction-fixed nystagmus. Changing of direction suggests a central lesion and fixed direction indicates a peripheral lesion.

8. Bithermal Calorics. Responses to cool and warm water or air stimulations are obtained for each ear. Calculations are made for the maximum speed of the slow component, duration of the nystagmus, unilateral weakness, and directional preponderance. The tracings are also evaluated for failure of fixation suppression, inversion, perversion and premature reversal. A unilateral weakness can only be caused by a peripheral lesion. Directional preponderance indicates either a central or peripheral lesion. Failure of fixation supression, premature reversal, inversion, and perversion are all central signs (Fig. 4).

With present day electroencephalographic equipment, electrical recordings may be made of the eye movements and these may be related to the stimulus to provide objective permanent records of the individual's labyrinthine responses.

Electronystagmography is a useful adjunct to the physician's armamentarium in the evaluation of dizziness and vertigo. It is not a test or procedure which renders unnecessary the usual careful history and medical investigation or the specialized examination of the ear, but it serves as a useful adjunct to these and has become part of the functional examination of the internal ear.

The three specific advantages of this physiological examination are that:

1. The ear is tested with minimal or moderate stimulation and should be expected to respond in a somewhat normal fashion.

2. The nystagmogram, as recorded by the electroencephalographic type instrument, is recorded as a permanent written record of the presence or absence of any nystagmus.

3. These written tracings allow for leisurely evaluation and comparison with subsequent tests, which provide an opportunity for long term follow up. It is practical, from the tracings, to derive quantitative measurements of the intensity and direction as well as the duration of the nystagmus.

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Dietary Fiber and Fiber Supplements in the Therapy of Gastrointestinal Disorders

JOHANNA T. DWYER, D. SC., BARRY GOLDIN, Ph.D., SHERWOOD GORBACH, M.D.
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ABSTRACT

Dietary fiber supplements may relieve symptoms of constipation, spastic colon, and diverticular disease; in the two latter disorders, colonic pressure relationships are altered. However, current evidence does not support other therapeutic uses for dietary fiber constituents, except possibly in patients with anal fissures and hemorrhoids, which can be helped by the passage of a softer stool.

"Roughage" and "dietary fiber" are receiving increasing attention, largely due to the belief that lack of fiber in the contemporary diet may be causally linked to several chronic diseases, and that dietary fiber supplements may prevent or ameliorate these conditions. This review considers the sources, composition, and properties of dietary fiber. The physiological actions of dietary fiber and the evidence for its role in preventing or treating gastrointestinal disease are examined.

SOURCES, COMPOSITION, AND PROPERTIES OF DIETARY FIBER

Sources of Dietary Fiber

Dietary fiber is usually defined as that part of whole grains, vegetables, fruits, seeds, and nuts that resists digestion in the small intestine (Table 1). Most dietary fiber is contained in various plant foods, such as fruits, vegetables, and some cereal products. Food fractions particularly high in dietary fiber may also be consumed — e.g., various bran fractions derived from the milling of wheat. Some processed foods contain synthetic or naturally-occurring gums (hydrophilic colloids) which also contribute to dietary fiber intake. Bulk-producing hydrophilic colloids, such as psyllium hydrophilic colloid (Metamucil®), are chemically similar to dietary fiber and are widely used as laxatives.

Comparability of Different Sources of Dietary Fiber

Naturally-occurring dietary fiber sources can have a variety of chemical structures and physicochemical properties[1] (Table 2). It is possible to analyze foodstuffs for their chemical constituents, but the origin of substances excreted in the feces is difficult to determine. Laboratory fractionation of fecal material into bacterial residues, undigested food, and endogenous secretions is a relatively primitive scientific technique. Thus, it is nearly impossible to assess the quantitative contributions of different sources of dietary fiber to each of these factors. Certain components of fiber, such as hemicellulose, are broken down by the bacteria in the large intestine and subsequently digested. Some food constituents, such as fatty acids produced by bacterial flora from some fiber components, may be absorbed in the colon and disappear. Such phenomena cast doubt upon definitions of dietary fiber based on non-digestibility.

The digestibility of the unavailable carbohydrates present in dietary fiber also may vary among individuals depending upon differences in the extent of biotransformation by the secretions of the digestive tract or by intestinal bacteria.

Quantity of Dietary Fiber in Foodstuffs

Dietary fiber is chemically analogous to "unavailable carbohydrate" — cellulose, hemicellulose, and pectins. These substances are the structural polysaccharides of the cell.[2] Dietary fiber also includes certain non-carbohydrate substances, such as lignins, waxes, cutins, etc.[1] Unfortunately, neither of the two values commonly used in nutrition tables for carbohydrates — net metabolically utilizable carbohydrate and crude fiber— gives usa-

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Table 1

Characteristics of Dietary Fiber

Form in Which Fiber Appears	*Name*	*Chemistry*	*Absorb Water or Water-Soluble?*	*Degraded by Intestinal Bacteria?*	*Other Characteristics Relevant to Clinical Medicine*
1. Dietary fiber naturally present in foods	Components of plant cell walls:				
	Pectin	Complex polymer of the sugar uronic acid and its derivatives	Yes	Yes	Form gels and thus alter water holding capacity of residues. React with metal ions such as calcium to form insoluble pectates; this may influence nutrient absorption.
	Hemicelluloses A and B	Structural polysaccharides composed of glucose units	Yes	Yes	When attacked by intestinal bacteria, produce volatile short chain fatty acids (acetic, butyric, propionic). In addition to organic acid production, metabolism of hemicellulose by gut flora leads to increased stool water loss, increased fecal fat, and nitrogen excretion.[14]
	Cellulose	Structural polysaccharides composed of glucose units	No	Yes	
	Lignins	Heterogeneous, amorphous, random polymers of phenylpropane units making up the skeleton of the plant	No	No	Absorb bile acids, particularly secondary bile acids such as deoxycholic acid. Degree of polymerization (lignification) depends on age, type of plant, etc., so lignins differ considerably even if from the same source.[6] These differences in lignification affect the digestibility of the celluloses present in food.
	Components found elsewhere in plants:				
	Waxes, cutins, etc.	Unavailable lipid substances forming part of skin or rind of plant	No	No	
	Materials found associated with dietary fiber	Unavailable nitrogen, trace elements, enzymes, minerals, salts, etc., present in vegetable cell walls[3]	—	—	
2. Food fractions particularly high in fiber	Brans, husks, germs of various cereals		See Tables 4 and 5		
	Naturally occurring gums[53]	Unavailable polysaccharides, colloids	Yes	?	Dissolve or disperse in water to make a viscous mucilaginous solution or suspension.
	Carageenan (Irish Moss extract)	Unavailable polysaccharides, colloids	Yes	?	Water extract of certain red algae seaweeds. Seaweeds themselves are used in the Orient.
	Aginic acid, algen	Unavailable polysaccharides, colloids	Yes	?	Extract from brown algae.
	Agar	Unavailable polysaccharides, colloids	Yes		Seaweed derivative often used for making sweetened, flavored gels.
	Furacellan	Unavailable polysaccharides, colloids	Yes		A seaweed extract.
3. Additives providing fiber sometimes present in processed foods	Naturally occurring gums (see above)				
	Synthetic gums	Unavailable polysaccharides existing in a colloidal form	Yes	?	These substances have been approved by the Food and Drug Administration for use in foods, but if they are used as dietary supplements the amounts used may

Characteristics of Dietary Fiber

Form in Which Fiber Appears	*Name*	*Chemistry*	*Absorb Water or Water-Soluble?*	*Degraded by Intestinal Bacteria?*	*Other Characteristics Relevant to Clinical Medicine*
					surpass approved levels. Therefore they are not presently recommended for supplement use.
	Avicel	Microcrystalline cellulose			
	CMC	Carboxymethyl cellulose			
	Methylcellulose	Cellulose derivative			
	Hydroxymethylcellulose	Cellulose derivative			
	PVP	Polyvinyl pyrolidine			
	Carbopal	Polyvinyl polymer			
	Polyox	Polyethylene oxide			
	Gantrezan				
4. Bulk producing hydrophilic colloids	Psyllium hydrophilic colloid (Metamucil)	See Tables 4 and 5	Yes	?	

ble data for determining the dietary fiber content. Carbohydrate values of foods are not determined by direct analysis but rather by difference and hence are subject to considerable error. Crude fiber values (what is left after acid and alkali extraction) underestimate the quantity of all dietary fiber and completely ignore the pectin substances.[3,4] Thus, food table values are underestimates.

Dietary Fiber Intakes

Most American adults consume 4 to 5 g of crude fiber daily. Figures for dietary fiber intake are more difficult to determine, but the average American diet probably provides 10 to 20 g of dietary fiber. Intakes in other industrialized countries are of this same order.[5] In contrast, among vegetarians or semi-vegetarians, both in this country and abroad, daily intakes may approach 10 g of crude fiber or 25 g or more dietary fiber.

Constituents of Dietary Fiber and How They Vary

The dietary fiber components of foods are associated with plant cell walls that normally contain chemically inert cellulosic fibrils embedded in a matrix of pectins and hemicelluloses. The framework of mature cells is further encrusted with lignin.[6] Dietary fiber components of plants change as the plant grows. The cell walls in young plants are thin and composed largely of cellulose and pectins, while those in aged plants are usually thicker and have higher hemicellulose and lignin contents.

The chemical composition of the dietary fiber present in foods will also vary with alterations in botanical variety, cultivation practices, weather conditions prior to harvest, ripeness, and storage. Such differences may have large effects upon physiological properties.

Physiological Actions of Dietary Fiber

Neither the physiologic effects of dietary fiber (Table 3) nor the relation of fiber to human health and disease (Table 4) are adequately understood. Physiological effects may actually be due to fiber or, alternatively, to materials occurring with or derived from fiber. For example, intestinal gas production or flatus is known to be increased when some vegatable foods are ingested. The raffinose and stachyose (tri- and tetra-saccharides) content of brussels sprouts and beans, rather than their fiber content, have been implicated as the cause. Yet production of other gases, such as hydrogen and carbon dioxide, is associated with bacterial action on nonabsorbable fermentable substances in the diet. Methane production requires large numbers of certain colonic bacteria which may be a familial trait affecting about one-third of the population. Among such persons, increased dietary fiber may lead to more flatus.[7].

Table 2

Definitions of Terms Used to Describe Components of Dietary Fiber

Term	*Definition*
Available carbohydrates	Carbohydrates that are absorbed from the small bowel.
Unavailable carbohydrates	Carbohydrates that are not thought to be absorbed from the small bowel (pectins, hemicellulose, cellulose).
Dietary fiber	All unavailable carbohydrates plus lignins.
Crude fiber	Hemicellulose, cellulose, lignins, synthetic non-nutritive fiber.
Synthetic non-nutritive fiber	Cellophane, cellulose from wood pulp, and methylcellulose.

Ancillary substances rather than the dietary fiber itself thus may explain physiological effects (such as serum lipid lowering) of dietary fiber sources. For example, such a component was responsible for the hypolipidemic effects seen in rats fed the husk of bran or paddy rice.[8] The saponin content, rather than the dietary fiber content, of alfalfa has cholesterol-lowering effects in experimental animals, reducing both the absorption of endogenous and exogenous cholesterol by formation of insoluble complexes in the gut.[9,10]

Purified sources of dietary fiber that can be chemically and physically defined include such materials

Table 3

Postulated and Observed Effects of Bran

Claim	*Status of Evidence and Comments*
Increased fecal weight	Demonstrated. The use of a heaping tablespoon of bran (about 1.5 oz.) has been used to improve bowel function by increasing fecal weight. Possible explanations include absorption of water and cathartic effects related either to volatile fatty acids produced in the large intestine from bacterial action or the sequestration of bile acids and fatty acids within undigested fiber particles which are then liberated as the fiber is partially metabolized by the gut flora.
Decreases intestinal transit time	Inconclusive.
Increased frequency of defecation, at least in subjects who are "normal"	Demonstrated and generally accepted, but mechanism is not entirely clear.
Alteration of fecal bile acid and cholesterol in the bile	Demonstrated but mechanism is less clear. Production of primary and secondary bile salts is altered. Deoxycholate (a secondary bile salt) decreases and chenodeoxycholate (a primary bile salt) increases. The total bile salt excretion may remain the same. Synthesis of chenodeoxycholate may increase while that of cholate is unchanged with total bile salt synthesis tending to increase.
Decreases intraluminal pressures in colon	Equivocal. Differences in findings may be due to: (1) use of different kinds of bran which vary in ability to absorb water, (2) differences in the state of the colon (full or empty). If effect exists, it may be due to bran, bulk, humoral, mechanical, or biochemical changes, altered bacterial flora, dilution of a spasmogen, etc.
"Normalizes" colonic activity; making very rapid transit times shorter and very slow transit times faster	Inconclusive. May be largely a placebo effect, especially among constipated patients.

Table 4

Hypothesized Associations Between Dietary Fiber and Reduced Frequency of Specific Diseases

Disease	*Mechanisms and Strength of Evidence for Proposed Mechanism*
Dental caries	High fiber "scrubs" teeth because it is coarse. Diets high in fiber are often low in sticky sweets. Therefore, an indirect mechanism is proposed. Evidence is fairly conclusive.
Hiatus hernia, diverticular disease, appendicitis, ulcerative colitis, irritable colon syndrome	Fiber may bind water and otherwise increase bulk of the digesta, therefore decreasing intracolonic pressure and improving intestinal "tone." Evidence is suggestive for irritable colon and diverticular disease, and weak for the others.
High cholesterol or triglyceride levels, coronary thrombosis, gallstones	Based on fiber's ability to absorb materials influencing serum cholesterol and bile acid metabolism. Evidence is weak.
Benign and malignant tumors of the gastrointestinal tract, especially the colon and rectum	Fiber may bind with carcinogens, decrease transit times, or alter prevalence of precursor disorders conferring high risk. Evidence is weak.
Decreased mineral absorption	High fiber diets are also high in phytates. Phytate binding or complexing of minerals in the gut may decrease absorption. Mechanical erosion of the mucosal surface may increase losses of endogenous material. Evidence is fair to weak.

as defatted carrot fiber, bean fiber, wheat germs, and brans with specified fiber composition and extraneous materials removed. The availability of these clearly defined substances is analogous in importance to the development and use of purified diets in early nutritional research. Such diets permitted the identification of elusive dietary factors, i.e., vitamins. Naturally-occurring sources of dietary fiber are often contaminated with a number of other substances which may have nutritional significance either to mammalian or microbial metabolism. A purified source of dietary fiber is more uniform in composition, thus simplifying the identification of cause-and-effect relationships to physiologic changes.

Quantitative Changes in Bowel Function: Fecal Bulk

Fecal bulk is increased in parallel with dietary fiber.[11,13] Table 5 reviews some of the common hydrophilic bulk-forming agents and high-fiber content foods used in clinical practice. Many years ago Williams and Olmstead[14] showed that dietary fiber supplements clearly produced larger stools (50 to 100% or more) when added to a basal diet which was nearly devoid of cellulose and lignins. Increases in fecal weight depended greatly on the hemicellulose content of the supplement. When lignin constituted a large proportion of total nonassimilable carbohydrate, less hemicellulose and cellulose disappeared from the gut. The greatest increment in fecal weight was achieved when agar was added to the diet. Carrots and wheat bran had an intermediate effect, while cotton seed hull and cellu flour had no effect on stool weight. In both experimental animals and man, a given dry weight of agar, carrots, cabbage, and bagasse increases stool weights more than do bran, lucerne leaf meal, or cellulose. These differences are due to the water-absorbing ability of the former substances. Thus, similar bulking properties cannot be automatically expected from naturally-occurring fibers that are already hydrated.

The increase in fecal bulk observed when dietary fiber is added to diets is much greater (e.g., one to

TABLE 5

COMMONLY USED HYDROPHILIC BULKING AGENTS AND FOODS HIGH IN FIBER

Chief Constituents	*Preparation and Presentation*	*Comments*
Wheat Bran		
A by-product from the milling of wheat to make white flour. Contains about 20% fiber and variable amounts of nutrients.	Wheat brans differ in fiber, mineral, protein, and carbohydrate content depending upon extraction rate. Miller's bran or Donkey bran is 6% cellulose, 24% hemicellulose, 4% lignin. It is usually fed to animals. Fine bran powder has less water binding capacity and is 10% cellulose, 10% hemicellulose, 3% lignin. Coarse bran has intermediate water binding capacity and is 15% cellulose, 15% hemicellulose, 5% lignin.	Physiological effects are influenced by factors such as particle size.
Whole Grain Cereals	Cereals highest in fiber are Kellogg's All-Bran, Bran Buds, Nabisco 100% Bran, supplying 1.8 to 2.3 g crude fiber per ounce of wheat bran. Other cereals fairly high in fiber are Familia (1.1 to 1.3 g), Post's or Kellogg's 45% Bran Flakes and Raisin Bran (0.8 to 1.1 g).	Eaten as cereals in the United States.
Corn Meal		
A dietary staple in some developing countries (Africa, Latin America). Corn germ meal, maize meal, and fractions of corn meal vary in proportion of lignin, cellulose, and hemicellulose	Mixture available from Vitamins, Inc., Chicago, Illinois, consists of 0.2% lignin, 48% hemicellulose, 16% cellulose, 1% fat, plus ash and protein; water holding capacity is similar to wheat bran. If corn cob is added, lignin content increases.	Not popular among most ethnic groups in the United States.
Dried Carrot Powder		
Often sold in health food stores	Type sold in health food stores may not be defatted. Therefore carotene levels may be extremely high, even dangerously so; carotenemia may occur. A defatted preparation is available from Vitamins, Inc., which has most of the carotenes removed. Its composition is 2% lignin, 25% cellulose and 1% hemicellulose. Natural sugars and 3 to 5% of solids remain in the product.	Gummy
Semisynthetic Cellulose Ethers		
Prepared from wood or cotton celluloses in various grades of viscosity	Cologel liquid (Lilly), Hydrolose syrup (Upjohn)	Taken with water.
Mucilaginous Seeds and Seed Coats		
Mostly from plantago ovata species, e.g., psyllium and ispagnula husk. These seeds contain a large amount of natural mucillage and form a gelatinous mass on contact with water	Konsyl powder (Burton, Parsons), Effersyllium powder (Stuart), Metamucil powder (Searle), Mucilose flakes and granules (Winthrop), Siblin tablets (Parke, Davis)	Predispersed in water and taken with additional water. Usual dose is 7 grams per day.
Mucilaginous Gums		
Karaya gum (sterculia) contains hydrophilic polysaccharides	Movicol (Norgine)	Granules placed dry on tongue and swallowed with plenty of water. This bulk agent has never been known to cause obstruction.

Preparations of Marine Algae

Agar and other preparations have been used as laxatives but they are relatively ineffective.

Foods High in Fiber

Foods high in fiber include any whole grain bread products, cereals, whole grain crackers, bran, raw and dried fruits, vegetables and berries (especially those with stalks and stems or skins), dried peas, beans, lentils and corn, nuts and seeds (e.g., sesame seed, sunflower seeds). The list below gives highest content in each group.

Vegetables:	1.5 g crude fiber or more per usual serving: artichokes, bamboo shoots, lima and kidney beans, bean sprouts, broccoli, brussel sprouts, cabbage, carrots, cauliflower, chick peas, collards, corn, cowpeas, cucumbers, dandelion greens, escarole, kale, kohlradi, leeks, lentils, okra, peas, peppers, radishes, rutabagas, soybeans, squash, turnip.
Fruits:	2.0 or more g crude fiber per usual serving: blackberries, blueberries, boysenberries, currants, watermelon. 1.0 g crude fiber per usual serving: apple, apricots, avocado, cherries, cranberries, figs, grapes, mango, papaya, pineapple, plums, prunes, raisins, strawberries.
Miscellaneous High Fiber Foods:	1 g per serving: Jell-O chocolate ready-to-serve pudding, fruit pies, green pea soup, chunky vegetable soup.
Breads and Cereals:	1.0 g crude fiber per serving: cracked wheat cooked cereal, 40% bran flakes, Grapenuts, Kellogg's All Bran, Bran Buds, Nabisco 100% Bran, Raisin Bran, bran muffin.

eight times) than the dry weight of the added fiber itself. This depends chiefly on the gel-forming ability of the fiber. Much of the increased bulk in healthy subjects represents water, especially entrapped water (found in the interstices of dietary residue) and gel or nonsolvent water (intimately associated

with dietary residue). However, swelling power in vitro and in vivo do not correlate well.[15]

Qualitative Changes in Bowel Function

The following qualitative changes in bowel function have been related to dietary fiber: softer stools,[3] greater frequency of bowel movements,[3] and decreased transit times.[16] These effects vary with the source and amount of fiber used. Sources of fiber in turn vary in proportions of undigestible components, their ability to absorb water, the extent of metabolism by gut flora, including production of volatile short chain fatty acids (which have osmotic and direct cathartic activity), and in the binding of bile acids or fatty acids which may be sequestered in the fiber particles during digestion and subsequently liberated.

Effects on Bowel Habit and Laxation

Bulking and softening effects of fiber are largely attributable to their ability to hold water, although some fibers may have direct cathartic activity. Data comparing the bulking effects of dietary fibers with other natural laxatives, such as methylcellulose and psyllium seed derivatives, are not available.

The effects of high fiber intakes on bowel habits are most notable among vegetarians, who often report an increase in size and frequency of bowel movement[17] and frequently complain of transient problems with gas and bloating, particularly if the diet is high in legumes.

Other Physiological Effects of Dietary Fiber on Gastrointestinal Function

Dietary fibers may influence a number of other functions that determine how food passes through the gut, including muscular contractility of the colon, intraluminal pressure, and possible mixing and streaming due to heterogeneity of fecal contents.[18] These functions may be of therapeutic utility in diverticular disease of the colon.

"Regularization" of bowel habits with dietary supplements of about 30 g of unprocessed bran per day have been reported by Harvey, Pomare and Heaton.[19] Individuals with rapid transit times slowed down, while those with slow transit times speeded up on these diets. However, transit times are extraordinarily variable: bran increases transit times in some studies and has little effect in others.[20] Alterations in transit times can also occur in constipated subjects after treatment with placebo.[21]

In summary, diets somewhat higher in dietary fiber than those consumed in this country increase fecal bulk. Dietary fiber supplements as well as alteration in food choices may accomplish this. One ounce of several commercially available cereals (Kellogg All-Bran or Bran Buds, or Nabisco 100% Bran) provides about 2 g of crude fiber (or probably twice this much dietary fiber). A tablespoon of crude miller's bran provides roughly 5 to 10 g of dietary fiber. Consumption of 15 to 30 g of dietary fiber in excess of that usually present in the diet is probably sufficient to achieve effects on fecal bulk and stool softness. Some believe that bowel habits, like halitosis, may be an issue of greater concern for psychological or social reasons than for health. However, to the extent that dietary fibers produce a feces more consistent with what patients consider "normal" and do away with the need for laxatives and cathartics, increased intakes may be desirable. In contrast, other experts believe that bowel habits are of fundamental importance in the causation of disease, and for them, increasing fecal bulk to approximately 150 g represents a prophylactic goal.

Effects on Nutrient Absorption

High fiber diets are associated with small, but definite, fecal loss of protein, fat, and carbohydrate.[22] However, Walker[23] observed relatively little effect of fiber supplements on nutrients among South African school boys who were already existing on high fiber diets. Their large stools were composed almost wholly of endogenous products, and frank malabsorption was not clinically evident.

Alterations in mineral absorption have been associated with dietary fiber. A variety of fiber sources fed to rats augmented calcium absorption and decreased iron and copper absorption.[24] In human volunteers eating usual American diets with fiber supplements, preliminary studies failed to indicate a decreased availability of calcium and zinc, but Fernandez, et al[25] observed fecal losses of potassium, sodium, and organic acids.

Phytic acid (inositol hexaphosphoric acid) is a constituent of most cereal grains. It forms insoluble salts (phytates) with minerals such as calcium, magnesium, and zinc and may prevent their digestion and absorption. Among vegetarians and health food users, the addition of dietary fiber supplements to a diet already high in phytates and bulk may lead to increased excretion of minerals. However, the experimental evidence in humans is not yet conclusive.

Effects on Colonic Flora

As much as half of the dietary fiber in Western diets potentially can be broken down by bacterial enzymes to produce short-chain fatty acids, water, carbon dioxide, hydrogen, and methane. The amount of bacterial degradation depends in part on the type of fiber present. Fiber appears to have lesser effects on fecal microbial populations than it does in altering the metabolic capabilities of the resident flora.

Effects on Lipid and Bile Salt Metabolism

Eastwood[26] has summarized studies on the influence of dietary fiber on bile salt metabolism. Populations that consume diets high in saturated fat and animal protein excrete large amounts of bile acid metabolites in their stools. Dietary fiber increases

fecal bile salt excretion in some studies but not in others. Pomare, et al[27] have shown that even if dietary fiber does not alter bile salt output, it may alter bile salt metabolism. Eastwood and Hamilton[28] demonstrated that bile salts were strongly adsorbed by the lignin component of various dietary fibers; the more polar the bile acid, the weaker the affinity. Secondary bile acids (deoxycholic and lithocholic) are probably adsorbed to dietary fiber more than primary bile acids. The pH of the residue passing down the gut may influence such binding, since it affects the ionization of acidic substituents on the fiber, as may the amount and methylation of the lignin present. In a study involving human volunteers on a Western type diet, Pomare et al[27] demonstrated that feeding a two-ounce supplement of wheat bran decreased the cholesterol saturation of bile, apparently by increasing hepatic synthesis of chenodeoxycholic acid.

Dietary fiber theoretically may alter bile salt and lipid metabolism through a variety of mechanisms — increasing fecal excretion of bile salts, altering the metabolism of bile salts so that cholesterol synthesis falls, and the preferential binding of deoxycholic acid to fiber. Although the mechanisms are not fully elucidated, bile salt excretion in man is probably affected differently by various fiber sources.

Dietary Fiber and Gastrointestinal Disease

The use of high fiber regimens for irritable bowel syndromes and diverticular disease is based on several theoretical concepts. A low fiber diet results in a hard, marble-like, fecal mass, small in volume and difficult to propel through the colon. Because of "overwork" the bowel musculature hypertrophies, especially in the sigmoid colon. The muscle thickens and the longitudinal muscles are thrown into ridges, with gaps in between. The diameter of the colon lumen narrows. As a result of these adaptations, high intraluminal segmental pressures develop in the colon. It is postulated that pulsion diverticulae form as the mucosa herniates through the gaps in the circular muscular coat, usually at the point of entry of blood vessels.

Grimes[29] has proposed that the type of disease depends upon the strength of the spasm producing increased pressure in the colonic lumen and the length of time the colon has been so affected. According to this view, irritable bowel precedes diverticular disease.

At present there is little proof for these theories or of a relationship between fiber in the diet and these diseases. Yet fiber proponents counter that in populations where people have fiber-rich diets and pass large, soft stools the prevalence of diverticular disease is low. Also, where populations have adopted a low fiber diet, within a generation increased prevalence of diverticular disease has been observed. Similarly fiber proponents maintain that the type of irritable bowel syndrome associated with raised intracolonic pressures and that associated with thickening of the bowel muscle coat also follow the same geographical distribution. But the fact remains that epidemiologic evidence does not establish causality.

Functional Bowel Disease

This common yet ill-defined syndrome has been called irritable bowel syndrome, functional bowel disease, spastic colon, mucous colitis, and spastic colitis. The syndrome is usually characterized by abdominal pain and mucous in the stool, and diarrhea, often alternating with constipation. Bland, "low residue" or "low roughage" diets traditionally have been prescribed to patients afflicted with this condition. Such diets often prove to be worse than the disease itself in terms of patient acceptance. Lately, high fiber diets have gained popularity based on the supposition that they will lower intraluminal pressures.

Gut wall tension in irritable colon is thought to be increased because of the spontaneous contractile activity of the muscular coats. Dietary fiber may aid in propulsion of the feces and decrease the strength of spontaneous contraction by augmenting stool bulk while not distending the bowel so acutely as to give rise to pain.

In a four-month clinical trail, 77% of Piepmeyer's[24] thirty patients with the irritable colon syndrome reported symptomatic improvements on 100 g of bran per day. Reported benefits included increased fecal bulk, more formed feces, more regular bowel habits, and decreased abdominal distention, cramps and anxiety. However, a large placebo response is common in this disorder, and a control group was not included.

Functional diarrhea is thought to be associated with an increased phasic activity and contraction in the distal segments of the bowel. It is exaggerated by food and emotional tension.[30] Dietary fiber would be expected to aggravate the diarrhea and to be contraindicated. Therefore, this condition must be distinguished from irritable bowel syndrome.

The best clinical trail to date of the effect of bran on irritable bowel syndrome is that of Soltoft and associates.[31] Fifty-nine outpatients participated in a six-week randomized double-blind trial. The experimental group received wheat biscuits of similar appearance to those of a high-bran type of biscuit furnishing 30 g bran per day. Fifty-two percent of the patients in the experimental group as opposed to 65 percent in the control group noted subjective improvement, thus providing little support for the use of miller's bran in irritable bowel syndrome. However, patients with both diarrhea and constipation, or combinations of these, participated in the trial, and all patients who were severely constipated were advised to use laxatives. Also, bran biscuits may pass as a bolus through the gut, whereas an equivalent amount of bran taken in smaller quantities throughout the day might have a more pro-

nounced effect on bowel habit.

Thus, there is little evidence to support the use of high fiber regimens for irritable colon characterized by constipation, and little or no evidence that it is of value for functional diarrhea. No diet or dietary supplement is established as therapeutic or symptomatically useful in this disorder. The preventive roles of fiber are even less clear.

Diverticular Disease

Arguments favoring the possible value of dietary fiber in the prevention and therapy of diverticular disease of the colon are based upon theoretical justifications, descriptive epidemiological studies, animal experiments, and observations during and after medical and surgical treatment.

Epidemiological data show that diverticular disease is high in most industrialized countries and low in developing countries where diets are high in fiber. Further, it is claimed that disease rates are higher today in Great Britain than they were in the past when diets were presumably higher in fiber.[32] However, the incidence of diverticular disease varies even among populations consuming high fiber diets in developing countries.[33] Antia and Desai[34] have claimed that a high proportion of elderly Indians have colonic diverticula in spite of a high fiber diet. However, their population was a group of Parsees who eat a diet that is much lower in fiber than that of the average Indian. Thus, the association of colonic diverticula with fiber intake is not perfect. The correlation also is questionable because age-adjusted rates were not used for comparisons.

Rats fed low fiber diets tend to develop diverticula of the colon, and the caliber of the large bowel is narrower at necropsy. In human studies, diverticular disease is marked by a seemingly exaggerated response of colonic intraluminal pressure to stimuli such as food and neostigmine.[35,36]

In the past "low roughage", "low residue", and "bland" diets have been prescribed upon the assumption that such regimens are less irritating to the gut. While avoidance of seed, pits, etc., may be justified since these may become trapped in diverticula (although such substances are rarely found pathologically), there is little clinical evidence to support the "irritation" theory. Hydrophilic colloid supplements such as Metamucil and high fiber regimens have recently become popular, based upon the rationale that these substances furnish a pultaceous mass which acts as a physical buffer against excessive contraction. Diverticular disease can occur without muscle abnormality or notable bowel problems, particularly in the elderly. Conversely, muscle hypertrophy may exist without diverticular disease, and increased pressures and contraction may result from many causes. Increased dietary fiber may relieve some cases of painful disease: Mendeloff[7] believes these patients actually have irritable colon syndrome. But for other cases of diverticular disease in which nonpainful diverticula are present,

Librax®

Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br.

Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCl and/or clidinium Br.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants, and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Physical and psychological dependence rarely reported on recommended doses, but use caution in administering Librium® (chlordiazepoxide HCl) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) reported following discontinuation of the drug.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy. Advise patients to discuss therapy if they intend to or do become pregnant.**

As with all anticholinergics, inhibition of lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established.

Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated; avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment, blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, *i.e.*, dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

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fiber probably does little good.

Hodgson[37] found that methylcellulose supplements decreased high intraluminal colonic pressures, and brought clinical improvement to patients suffering from diverticular disease. Painter, et al[38] treated 70 patients between acute attacks of symptomatic diverticular disease (without fibrosis and irreversible narrowing of the lumen) with a high fiber diet consisting of bran supplements. Sixty-two of the patients that adhered to the regimen reported symptomatic relief (less abdominal discomfort) and decreased need for laxatives. None of these patients required surgery by the 22nd month of follow-up, while one of the dropouts did. Unfortunately, this was an uncontrolled experiment.

Devroede's randomized trial evaluated high and low fiber intakes for the treatment of diverticular disease.[39] A large (40%) placebo effect was observed on all regimens. Patients' reports of well-being were higher and symptom scores lower among those receiving Metamucil, a psyllium husk preparation, with no other special dietary suggestions. Metamucil is a concentrated hydrophilic colloid supplement similar to many other types of dietary fiber in its bulking properties. Thus, efficacy may have simply been related to the dose and type of fiber in supplements.

In the study of Findlay, et al,[40] a 20 g daily bran supplement decreased gastrointestinal transit times in all nine patients afflicted with diverticular disease as well as in normal controls, but the decrease was greater among the diseased group. Colonic motility and pressure did not change, but pressure did fall dramatically when neostigmine was administered.

Surgical procedures for diverticular disease, such as sigmoid colomyotomy or resection of the sigmoid colon, initially reduce intraluminal pressures. There is disagreement about the permanence of these changes. Some investigators claim permanent reductions, while others claim that intraluminal pressures gradually return to high levels, thus affording only temporary relief. One small series[41] suggests that if the postoperative diet is high in bran, pressures remain at a lower level for a longer period. Five postoperative resection patients and five patients who had myotomies for uncomplicated diverticular disease (e.g., continuing obstructive features, high colonic pressures, and thickened muscles) were prescribed bran and followed. After five years, the postoperative patients on the bran regimen all had lower intracolonic pressures and fewer clinical problems than twenty controls on nonbran prescriptions whose pressures gradually rose to very high levels. Results were particularly dramatic in the postmyotomy patients.

Therefore, for uncomplicated diverticular disease either before or after surgery, bran and hydrophilic colloids have been reported to be beneficial. High fiber foods seem less useful, perhaps because the quantity of fiber is less than in concentrated fiber supplements.

Other Gastrointestinal Diseases

None of the few studies have demonstrated conclusively that high fiber diets are useful in the prophylaxis or treatment of diseases unrelated to pressure, including ulcerative colitus, nonocclusive ischemic colitis, pseudomembranous colitis, and peptic ulcer disease. Burkitt[42] has suggested that a high fiber diet, by relieving constipation and high intraabdominal pressures, may prevent polyposis and relieve hemorrhoids. He also suggests that appendicitis is initially a pressure phenomenon following obstruction to the lumen of the appendix and that fiber may be useful prophylactically here as well. These uses remain conjectural.

Diet and Colon Cancer

An attractive explanation for geographical variations in the occurrence of colon cancer is differences in diet. In geographical areas of high colon cancer incidence, the population consumes large amounts of animal protein and fat. In areas of low incidence, including many developing countries, inhabitants consume a diet containing a large proportion of vegetables, cereals, and fiber. Several epidemiological studies strongly implicate diet as an etiological factor in colon cancer.[43-49]

At present, the major hypotheses being debated in nutritional circles are that: (1) differences in colon cancer incidence may be associated with variations in the fiber content of the diet, (2) differences in incidence are associated with the type of lipid and/or protein in the diet, and (3) toxic substances in the diet cause increased tumor development.

Burkitt hypothesis: dietary fiber deficiency. Dietary fibers clearly influence intestinal function, although what functions are affected and the mechanisms of the effects are largely unknown. More controversial is the argument of Burkitt[42] and others that deficiency of dietary fiber is an associative cause in the pathogenesis of colon cancer as well as in a number of other diseases.

In his study of the diet of Africans, Burkitt[42] concludes that unabsorbable fiber content is the most notable difference between African and Western diets. He also claims that since more unabsorbable fiber is consumed by Africans, they have more rapid intestinal transit times as measured by x-ray tracking of swallowed radiopaque markers. In English schoolboys, 80% of the markers passed through the intestinal tract within 89 hours. On the other hand, African villagers required only 35 hours to pass the markers.

Burkitt[47-49] suggests that high intakes of dietary fiber protect against colon cancer by several mechanisms. First, fiber dilutes intestinal residue and any potential carcinogens formed by bacterial degradation. Second, dietary fiber decreases transit times, thus allowing less time for carcinogens to be produced and remain in the bowel.

Ershoff[50] coined the term "antitoxic" to refer to the protection that is seemingly afforded by some

dietary fibers against noxious substances of exogenous or endogenous origin. Neither cellulose content nor hypocholesterolemic activity explains the differing effects of fiber in this regard. Whether this "antitoxic" activity is related to physicochemical binding in fiber interstices or gel or whether there is a change in the intestinal milieu (i.e., the microflora) is not known. However, metabolism by intestinal bacteria has been described for cyclamates, food dyes, and bile salts, all of which may be altered by dietary fiber sources. Even physical dispersion of the substrate or its products in the fecal mass may have important consequences in terms of mucosal contact time and absorption.

Criticisms of fiber hypothesis. Criticism of the "fiber deficiency" hypothesis as an explanation for the high prevalence of atherosclerotic disease in Western countries also applies to the postulated relationship for colon cancer.[51] That is, the studies rest only on epidemiological ground. Unfortunately, the circumstances of life and environmental factors, including the prevalence of infectious disease and chronic illness, vary tremendously between these same populations. Changes in dietary practices occurring with industrial and economic development tend to be similar, regardless of the geographical area in which they occur, and non-food factors may also change simultaneously.[51]

The emphasis has focused on bran, particularly wheat bran, yet in countries where rates of atherosclerosis and colon cancer are low, the vegetable fibers are not derived from wheat nor are they even necessarily of cereal origin.

Drasar and Irving[52] have suggested that dietary intakes of animal fat and protein correlate more closely with the incidence of colon cancer than does the negative relationship with dietary fiber. But the inadequacy of figures on fiber intakes at present make such statements difficult to support.

Persons subsisting upon vegetarian or vegan diets high in dietary fiber also differ from American omnivores in a number of other respects. Studies which assume that the only difference between vegetarians and nonvegetarians is intake of dietary fiber are immediately suspect.

Thus, the evidence that has been provided to support the "fiber deficiency hypothesis" is not sufficient to date to explain the complex etiology of colon cancer.

Adverse Effects and Contraindications

Concentrated sources of dietary fiber, such as bran, psyllium seeds, carrot powder, etc., should not be eaten dry because of possible esophageal obstruction or, more rarely, intestinal obstruction due to formation of a bolus. Natural sources in fruits and whole grain cereals do not present this problem since they already are partially hydrated or are eaten with liquids.

Very large doses of concentrated sources of fiber may well have an adverse effect on the absorption of

Tablets

Percodan® (II)

DESCRIPTION Each yellow, scored tablet contains 4.50 mg oxycodone HCl (WARNING May be habit forming), 0.38 mg oxycodone terephthalate (WARNING May be habit forming), 224 mg. aspirin, 160 mg phenacetin, and 32 mg caffeine.

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone, aspirin, phenacetin or caffeine.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCODAN®, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCODAN® is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCODAN® should be cautioned accordingly.

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCODAN® may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCODAN® should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCODAN® should not be administered to children.

Salicylates should be used with caution in the presence of peptic ulcer or coagulation abnormalities.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions The administration of PERCODAN® or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients PERCODAN® should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

Phenacetin has been reported to damage the kidneys when taken in excessive amounts for a long time.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient The usual adult dose is one tablet every 6 hours as needed for pain

DRUG INTERACTIONS The CNS depressant effects of PERCODAN® may be additive with that of other CNS depressants. See WARNINGS.

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2. Prescribe a rapid-acting agent

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3. Minimize potential risk

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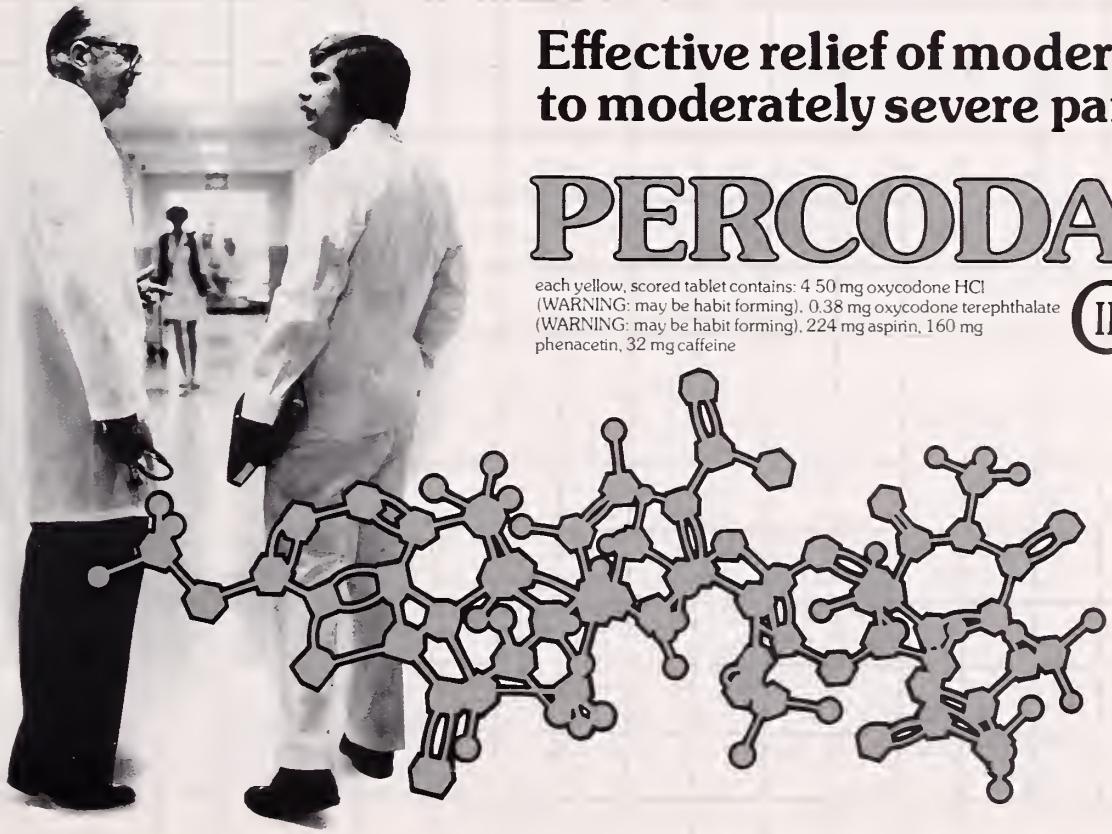

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certain minerals and trace elements such as calcium, zinc, and iron. Flatulence and distention may be temporary problems if large amounts of bran or beans are eaten by some patients.

Bulk-forming laxatives are contraindicated for those patients with ulcerative colitis or regional ileitis if, after therapeutic trial, they increase symptoms and diarrhea. Theoretically, they could produce obstruction if the lumen were exceedingly narrow. In acute attacks of diverticulitis, such dietary manipulation is potentially hazardous.

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McLEAN NAMED PRESIDENT-ELECT

The Blue Cross and Blue Shield of Maine Board of Directors has named George E. McLean to succeed Richard F. Nellson as President of the Plan in March, when Mr. Nellson will be retiring.

GEORGE E. MCLEAN

McLean was brought up in the Bangor, Maine, area and graduated from Bangor High School and the University of Maine at Orono. He was an officer in the U.S. Army in World War II and worked as an actuarial student and expense analyst with the Travelers Insurance Company before joining Blue Cross and Blue Shield of Massachusetts in 1956. He has been Vice President Actuarial/Underwriting Administration with the Massachusetts Plan for eight years.

He has been consulting actuary to the Maine Plan for over eight years. Among his many accomplishments in that capacity was the installation of experience rating of health coverage for the larger groups in Maine.

McLean is a member of the Equalization Committee of the Blue Cross and Blue Shield Associations (Chicago) and is Chairman of the Actuarial/Statistical Committee of District 1, of Blue Cross and Blue Shield.

Professionally, McLean is a Fellow of the Casualty Actuarial Society (by examination), and is a member of the American Academy of Actuaries, the American Risk/Insurance Association, and the International Actuarial Association.

In Massachusetts, he has chaired the Board of Public Welfare, the Insurance Advisory Committee, the Board of Trustees of Hopkinton Public Library, and the Annual Girl Scout Fund Drive. He served as Moderator of the First Congregational Church of Hopkinton from 1970-1975. He is currently chairman of his local Zoning Board of Appeals.

McLean, who summers in North Edgecomb, Maine, is married to the former Valerie Power, a Westbrook College graduate. He has two daughters, Susan J., who has a teaching fellowship at State University of New York at Binghamton, and Judith G., who is employed by Liberty Mutual Insurance Company in Boston.

Maine Department of Human Services

DAVID E. SMITH
COMMISSIONER

We Must Be Doing Something Right or We Must Be Doing Something, Right?

DENNIS J. DIX†

Arguments questioning the need to protect the youngster against rubella at 12 to 15 months of age come to the surface from time to time. The most common argument questions whether or not the vaccine confers long lasting immunity against rubella. According to these arguments, vaccine should be administered to peri-pubertal adolescents, particularly females of that age. Another school of thought down plays the role of children in the spread of rubella to the gravid female and ultimately to the unborn fetus.

The reported incidence of congenital rubella syndrome (CRS) has steadily declined since 1969.[1] During that year two significant events occurred. In mid-year, rubella vaccine was licensed, paving the way for large scale community programs and increased immunity levels. The decision to immunize the 1-9 population was made as a matter of Maine's policy. In addition, the Conference of State and Territorial Epidemiologists called for an extensive search for CRS affected children. The National Registry for Congenital Rubella Syndrome was established by the Center for Disease Control.

For calendar years 1970 through 1975 (the period for which data is available, the nationwide number of CRS children fell dramatically despite intensified efforts to ferret out new cases (see Table 1).[2]

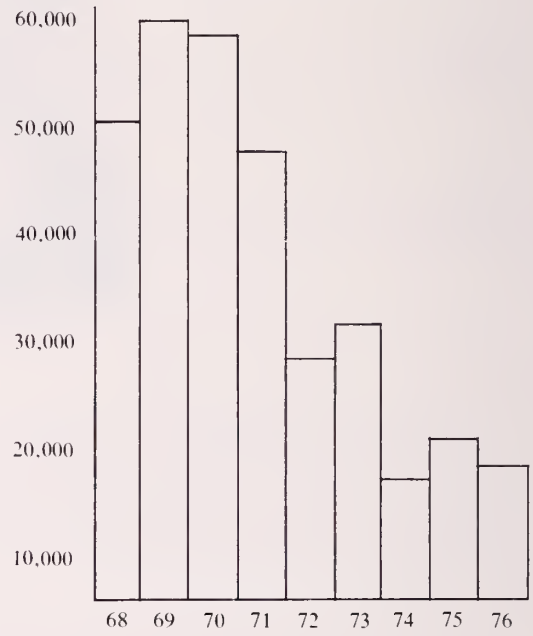
TABLE 1

CRS CASES REPORTED TO NRCRS

Years	*NRCRS Year of Birth**
1968	138**
1969	132**
1970	90
1971	52
1972	40
1973	38
1974	25***
1975	22***

*Figures differ from national morbidity and mortality data which is based on year of diagnosis.
**Based on a retrospective study.
***Numbers may have increased slightly since CRS is often not diagnosed for months following birth.

Figure 1
Reported Cases of Rubella, United States
1968-1976



Even more impressive is the dramatic decline in reported rubella morbidity from nearly 58,000 cases in 1969 down to 12,000 cases in 1976. With little exception the number of case reports has declined in each year compared to the previous year (see Figure 1). It should be noted that the six-to nine-year epidemic cycle was expected to peak between 1970 and 1973. The projected epidemic never materialized. Someone was doing something, right?

With regard to the maintenance of sero-positive rubella immune levels, the evidence leans toward confirming the hypothesis that the pattern of rubella HAI titers among those immunized parallels the HAI pattern following natural rubella infection.[4] It should be noted, however, that some studies indicate that HAI titers among immunized persons fall on an average of one or two dilutions below those infected by wild rubella virus.[5]

†Director, Immunization Program

The *raison d'etre* for rubella vaccine is the reduction and, hopefully, the elimination of, CRS. Whether you agree with the game plan or not, it seems to be working.

We believe that we can profit from the arguments presented by our dissenting colleagues: not by switching strategy, but rather by modifying current recommendations.

We believe that the current policy promoting rubella immunizations among the prepubertal population is a good one. Immunization against rubella should be given as soon after 12 months of age as possible. The prepubertal approach, however, excludes the relatively small percentage of women in the post-pubertal cohort who are still susceptible to rubella.

We suggest that physicians and/or hospitals consider adopting a policy under which seronegative females are immunized following the termination of pregnancy. This policy should be consistent with the rubella vaccine manufacturer's recommendations (e.g. contraception for three months following rubella vaccination).

We further suggest that post-pubertal females be screened for rubella immunity. Surveys demonstrate that approximately 15% of all females beyond 20 years of age will be sero-negative. Susceptible females could then be immunized consistent with recommendations governing this population.

In summary, someone's doing something right, hopefully we all can make it righter.

We would appreciate your comments, tel. (207) 289-3746.

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5. Based on the results of an unpublished study conducted in School Administrative District No. 22, Maine. HAIs were obtained from 294 females giving a history of rubella vaccine (confirmed without a history of disease and compared to 119 females with verbal history of disease without vaccine history). The Geometric Mean Titer for those with vaccine history only was 29.39 (mode: 1-32). The GMT for those with disease history only was 47.27 (mode: 1-128). Subjects with titers less than 1:8 were arbitrarily assigned a value of 1:4 for the purpose of this calculation.

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From the Secretary's Notebook

Summary of 1977 Fall Meeting of the M.M.A. House of Delegates

December 10, 1977 at Waterville, Maine

The Fall Meeting of the M.M.A. House of Delegates was held at the Mid-Maine Medical Center (Thayer Unit) in Waterville on Saturday, December 10, 1977, with an attendance of 58 delegates and alternates, and six guests. Douglas R. Hill, M.D., President of the M.M.A. called the meeting to order and George W. Bostwick, M.D., Speaker of the House, presided.

1. **Reports of Officers:**

a) Dr. Hill, President, explained the current status of the "Medicaid Cutback" suit and reviewed other legal and legislative matters of interest and concern to the members.

b) Dr. McAfee, Delegate to the AMA, reported on the convention held this week in Chicago. He served as Chairman of the Bylaws Committee and one of the items discussed was specialty representation in the House of Delegates. This same issue is to be considered at the Maine Medical Association's annual meeting next June. Membership figures for the AMA, as well as those in component societies, were given by Dr. McAfee, who stressed the importance of participation by all physicians in the country. The delegates' attention was called to a Summary Report of the National Commission on the Cost of Medical Care, which appeared in the 12/5/77 issue of *American Medical News*, and to the matter of Federal guidelines for health planning.

2. **Committee Reports:**

a) *School Health* — Dr. Eric Nicholas, Chairman, reported that the Committee has been asked by the Department of Human Services to review and comment upon school nurse programs and has been asked by the Department of Education and Cultural Services to recommend new programs re general health and sports physical exams. He asked that anyone having concerns in the area of school health to contact their district representative on the committee, and urged that physicians give support to local school districts.

b) *Health Care Financing* — Dr. Charles Lightbody, outgoing Chairman, submitted a written report and added that the committee had approved recommending that the M.M.A. group Blue Shield plan be upgraded from the present "D" to the "100% UCR". Representatives from BCBS were present to advise the delegates of the benefit and premium changes. A motion was made to accept the proposal, and it was so *voted*. The change is expected to become effective May 1, 1978.

c) *Allied Health Professions* — Dr. A. Dewey Richards, Chairman, reported that the Committee has been active, and welcomes referral of appropriate matters to them.

d) *Building* — Dr. John Wickenden, Chairman, explained that this report was his own, that the committee had not voted on it, but that the report had been discussed with the Executive Committee. He reported there was no acceptable land or rental space available within walking distance of the State House for relocating the M.M.A. offices. Class A rental space in Augusta would be approximately $25,000 annually ($6.50-$9.00 sq. ft.), with Class B space running $15,000 ($4.75-$6.50 sq. ft.). He said there are existing properties available at a cost of $80,000 minimum, with an additional $10,000 plus for remodeling expenses. Land is available at the Civic Center Complex — Dr. Wickenden favors a combination of two lots totaling 65,000 square feet costing $40,000. Cost of erecting a new building is estimated by Dr. Wickenden to be approximately $120,000. By comparison, land in Brunswick runs approximately $8,000 an acre, and rentals cost $5-7 per sq. ft. Buildings available for sale range from $60,000 up, plus remodeling costs. Dr. Wickenden said that he plans to check available land on the corridor between Brunswick and Augusta and will present 3 or 4 specific alternatives to the House of Delegates in the spring for consideration.

When funds were mentioned, Dr. Bostwick reminded the delegates that the House of Delegates had authorized the Executive Committee, in June 1975, "to issue an assessment of up to $100 per member for the purpose of capital improvement, if there is a need for it", and that collection will be instituted when the Executive Committee deems it necessary.

e) *Ad Hoc Committee on Malpractice* — Dr. Patrick Dowling, Chairman, was present, as well as Mr. John Schroeder and Mr. George Shattuck of the firm of Johnson & Higgins, who presented statistics from the recently-concluded captive insurance company feasibility study. A copy of Dr. Dowling's report was sent to each delegate. A resolution was presented to the delegates and will be referred to the June meeting of the House of Delegates.

3. **Resolutions** — Six resolutions were presented to the delegates (copies sent to all delegates on December 5, 1977), and all will be referred to the June 1978 meeting of the House of Delegates for action. The following resolutions will necessitate a change in the Constitution if approved, and are printed here as required for any amendments:

PROPOSED RESOLUTION SUBMITTED BY THE EXECUTIVE COMMITTEE
"To Extend Tenure of Past Presidents on Executive Committee"

WHEREAS: The 1977 House of Delegates directed that a proposed Constitutional amendment be prepared to enable the Executive Committee to enjoy the counsel of each Past President for an extended period,

THEREFORE BE IT RESOLVED: That Article VI of the Constitution shall be and is hereby amended to read as follows:

Article VI Executive Committee

The Executive Committee shall consist of the President, President-elect, Executive Director (if a member of the Association), Secretary-Treasurer (if a member of the Association), the delegate(s) and alternate delegate(s) to the American Medical Association, the Speaker of the House, one member from each District, and the immediate Past-President who may, at his/her option, remain a voting member of the Executive Committee in this capacity for a period not to exceed three (3) years. Nine voting members shall constitute a quorum.

PROPOSED RESOLUTION SUBMITTED BY THE EXECUTIVE COMMITTEE
"To Implement Specialty Society Representation in the House of Delegates"

WHEREAS: It is fitting that deliberations of the House of Delegates should benefit from the counsel of specialty societies,

THEREFORE BE IT RESOLVED: That Article V of the Constitution shall be and is hereby amended to read as follows:

Article V House of Delegates

The House of Delegates shall be the legislative and policy-making body of this Association and shall consist of 1) Delegates elected by the component societies, 2) the Secretary of each component society (if a member of the Association), 3) the members of the Executive Committee, 4) all past presidents of the Association, and 5) Delegates elected by active medical specialty societies recognized by the Executive Committee of this Association, provided that each member of the House have one (1) vote.

PROPOSED RESOLUTION SUBMITTED BY PISCATAQUIS COUNTY MEDICAL SOCIETY
"To Include the Chairman of the Committee on Health Care Financing in the Executive Committee"

WHEREAS: The Committee on Health Care Financing is the only standing committee of this organization to have both geographical and categorical specialty representation, and

WHEREAS: Negotiations with third-party payors have become of major importance to the conduct of business of this Association, and

WHEREAS: The business of this committee frequently requires immediate attention by the Executive Committee,

NOW THEREFORE BE IT RESOLVED: That Article VI of the Constitution, entitled "Executive Committee," shall be and hereby is amended by the addition, at the end, of the following sentence:

"The Chairman of the Committee on Health Care Financing shall *ex officio* be a non-voting member of the Executive Committee."

4. Other —

a. A communication from the Kennebec County Medical Association re "a more equitable **fee schedule** for Maine physicians" was read by Dr. Bostwick. No one from the K.C.M.A. was present to elaborate on this, or to request specific action, and it was ruled out of order by the Speaker.

b) Dr. Thomas Shields, delegate from Androscoggin County, invited Maine physicians to participate in an AMA **Seminar on Negotiations,** to be held in Lewiston, Maine, April 1 and 2, 1978. Registration will be limited to 30, and further information may be obtained from Dr. Shields at 416 Sabattus Street, Lewiston, Maine 04240.

5. Spring Meeting of the House of Delegates — Saturday, March 18, 1978.

6. Adjourned at 4:25 P.M.

PATRICIA A. BERGERON
Secretary-Treasurer

Seminar on Negotiations

April 1 and 2, 1978

Lewiston, Maine

Enrollment limited to 30 physicians.
Watch your mail for application form.
Recommended particularly for those in leadership roles.

County Society Notes

Penobscot

The November meeting of the Penobscot County Medical Society was held on November 15, 1977, at Sing's Restaurant in Bangor.

The meeting was opened by the President, Dr. Phillip G. Hunter, and the minutes of the October meeting were approved. The business meeting was somewhat abbreviated to allow sufficient time for the several speakers of the evening.

An open request was made to the Society for volunteers who might be willing to serve on the Arbitration Panel as a part of the medical malpractice arbitration section of the Maine Health Security Act, L.D. 727. Physicians were urged to participate in offering their services for this Panel as a step in alleviating the current malpractice crisis.

Two applications for membership were presented: Drs. Andrew W. Krasuski and Zenaida Q. Tana of Millinocket. Both were unanimously accepted.

There followed a very enlightening and informative discussion of the current professional liability insurance situation in Maine and the status of the feasibility study by Johnson and Higgins of Boston regarding a doctor captive insurance company for Maine. Mr. Jock McKernan, the M.M.A. lobbyist, Mr. George Shattuck, an actuarial consultant of the firm Johnson and Higgins, and Dr. Richard Leck, member of the Ad Hoc Committee on Malpractice Insurance of M.M.A., were the guest speakers. At the present time, with just over 50% of the doctors having responded to the questionnaire and with the statistical analyses done this far, it does appear feasible that such a doctor insurance company would be workable for the State of Maine. The consultants like to have about 70% of the doctors responding to the questionnaire before reaching a final decision and recommendation, however.

The meeting was adjourned at 10:45 p.m.

H. Clement Jurgeleit, M.D., *Secretary*

Lincoln-Sagadahoc

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset on December 20, 1977.

The President, Dr. Anthony J. Horstman, called the meeting to order at 8:55 p.m.; the secretary read the minutes of the November meeting, and the minutes were accepted as read.

Old business: Dr. Horstman asked for names of those members willing to serve on arbitration panels for malpractice cases. Drs. Schall, Oceretko, Richard Evans, Wilkoff, Bachrach, Bostwick, and Dixon signified their willingness to serve.

Dr. Horstman asked for votes on the applications for Active membership from Drs. Alice Cunningham and James Burgess of Brunswick. On recommendation of the Board of Censors, both applications were unanimously approved.

Dr. Richard Evans discussed the Interim Session of the M.M.A. House of Delegates December 10th in Waterville: the possible relocation of the M.M.A. office, addition of specialty representation to the House, and approval of the UCR contract for the M.M.A. Blue Cross/Blue Shield group policy. Dr. Leck spoke on malpractice insurance, a possible physician-sponsored professional liability insurance company, a special one-time $100.00 assessment for a new building, and a lawsuit involving the Department of Human Services and a 10% fee reduction under Medicaid.

Dr. Schall reported a proposed slate of officers for the Nominating Committee:

President: Dr. Aldo F. Llorente, Brunswick
Vice-President: Dr. P. Richard Cote, Bath
Secretary-Treasurer: Dr. George W. Bostwick, Newcastle
Delegates to the M.M.A. House of Delegates: Drs. Richard Evans, III and David W. Schall, both of Brunswick. Alternates: Drs. Gerry S. Hayes, Brunswick and Anthony J. Horstman, Boothbay Harbor
Censors: Drs. Samuel L. Belknap, Damariscotta, Carl R. Griffin, Jr., Boothbay Harbor and Elihu York, Brunswick
Program Committee: Drs. Frank O. Avantaggio, Jr., Damariscotta and William G. Wilkoff, Bath

Dr. Leck moved that the nominations be closed and that the secretary cast one ballot for the entire slate. The membership approved.

Dr. Wilkoff introduced Dr. James Smith, who presented a case of Legionnaires' Disease; Dr. Gerry Hayes, who showed slides of a case of keratosis palmoplantaris with eye involvement; Dr. Robert Dixon, who spoke on sputum cytologic screening and then he presented a slide show of mixed horrors.

George W. Bostwick, M.D., *Secretary*

Androscoggin

The annual meeting of the Corporators of the Androscoggin County Medical Association was held at No Tomatoes in Auburn on December 15, 1977. The meeting was preceded by a social hour and dinner.

The business meeting was called to order by the President, Dr. Charles A. Hannigan, with 68 members present and one guest.

The minutes of the October meeting were read and accepted as read. The treasurer's report was given by Dr. Frederick B. Lidstone, accepted and placed on file.

Dr. Thomas R. Shields reported on the forthcoming plan for the Negotiations Seminar which will be held at the Ramada Inn on April 1 and 2, 1978. It is estimated that for 30 registrants the cost would be about $75.00, including two lunches, a cocktail hour and four coffee breaks. Dr. Stephen A. Sokol also spoke on this matter.

Dr. Gilbert R. Grimes and Dr. Frederick C. Holler reported on the matters discussed at the recent meeting of the House of Delegates held in Waterville. The subject of fees related to Medicaid; malpractice insurance, and the relocation of headquarters of M.M.A. were discussed.

Dr. Grimes reported for the Nominating Committee. The slate of officers and councilors and delegates was as follows:

President: Dr. Jou S. Tchao, Lewiston
Vice-President: Dr. Lawrence A. Nadeau, Lewiston
Secretary-Treasurer: Dr. Kenneth P. Wolf, Lewiston
Councilor: Dr. Gerard L. Morin, Lewiston (term expires 1980)
Delegates to the M.M.A. House of Delegates: Drs. Stephen A. Sokol and Lawrence A. Nadeau, both of Lewiston (term expires 1980). Alternates: Drs. Barry D. Chandler and Donald H. Morgan, both of Lewiston (term expires 1980)
Councilor representative for 7th District to M.M.A.: Dr. Gilbert Grimes (term expires 1978)

The slate of officers was accepted unanimously and the secretary was instructed to cast one ballot. It was so done.

The meeting was turned over to Dr. James I. O'Sullivan who presented a humorous program.

Meeting to be held at No Tomatoes, January 17, 1978.

There being no other business, meeting adjourned at 9:40 p.m.

Frederick B. Lidstone, M.D., *Secretary*

Franklin

The Franklin County Medical Society met on January 3, 1978, and the meeting was called to order by the President, Dr. James R. MacMahon.

A report regarding the House of Delegates meeting December 10th was made by Secretary, Dr. Daniel K. Onion and Delegate, Dr. David S. Hurst. The County members were warned of a possible upcoming $100.00 per member building assessment.

The change in Chairmanship of the Health Care Financing Committee was announced. The current negotiations between this Committee of the State Medical Association and the State Health & Welfare Medicaid Office regarding fee schedules was explained.

The new Blue Cross/Blue Shield Plan for Maine Medical Association members was explained and the costs described. Several members of the Franklin County Medical Society expressed

a desire to sign themselves and their employees up for the Franklin Area Health Plan, as soon as it becomes commercially available this spring, since its costs for more comprehensive care are less than the new Blue Cross/Blue Shield premium.

The current status of the formation of a captive insurance company by the Maine Medical Association, for the purpose of providing malpractice insurance for physicians in the State of Maine, was explained. Dr. Onion has already invited Dr. Patrick Dowling, from Portland, to come to a future Franklin County Medical Society meeting to explain what is going on to the County Society.

The resolution proposed by the Committee for Care for the Disadvantaged to dissolve that Committee and the objections of the Executive Committee were explained to the group. Their thoughts regarding how the delegates in this Society should vote in June were also sought.

Finally, in response to Jeff Hollingsworth's request about the upcoming legislation the State Medical Society is concerned about, Dr. Onion announced that Dr. Eastman will contact the Jay Legislator, Dr. Onion the Farmington Legislator and Dr. Hunter the Kingfield Legislator.

No further business. Meeting adjourned at 10:00 p.m.

DANIEL K. ONION, M.D., *Secretary*

News, Notes and Announcements

Recent Advances In Neuro-Endocrinology

PHILADELPHIA — The American College of Physicians (ACP) will sponsor a three-day postgraduate course "Recent Advances in Neuro-Endocrinology," March 6-8, 1978, in Montreal, Canada.

The postgraduate session is one of approximately 45 to be sponsored by the ACP in the United States and Canada during the 1977-78 academic year. Their purpose is to give specialists in internal medicine and related fields an opportunity to review basic information and to find out what is new in medical diagnosis and therapy.

One of the prime activities of the Philadelphia-based American College of Physicians is the continuing medical education of practicing physicians. In addition to presenting postgraduate courses, the 40,000-member ACP also sponsors nearly 40 regional meetings, a four-day national scientific session and publishes the monthly journal, *Annals of Internal Medicine*.

The American College of Physicians postgraduate courses have been approved by the American Medical Association Advisory Committee on Continuing Medical Education and the Montreal course may be used to fulfill 20 hours of Category #1 requirements for the AMA's Physician Recognition Award.

The Montreal course entitled, "Recent Advances in Neuro-Endocrinology," is being planned by George Tolis, M.D.; co-directors: Frederick Naftolin, M.D. and Joseph B. Martin, M.D.

For further information, write to Registrar, American College of Physicians, 4200 Pine Street, Philadelphia, Pa. 19104.

American College of Allergists

The *34th Annual Congress* of the AMERICAN COLLEGE OF ALLERGISTS will be held April 1-6, 1978, at the Las Vegas Hilton Hotel, Las Vegas, Nevada.

A comprehensive review of clinical immunologic and allergic diseases relevant to the needs of the physician in practice. The 5½-day program will focus on physician/registrant participation.

Credit: AMA C.M.E. Category I — 30 hours.

Registration fee: Members — $75; Non-members — $190.

No fee for Residents, Interns, Nurses and Technicians from teaching hospitals, presenting letters from department heads.

INFORMATION: Frances P. White, Executive Secretary and Treasurer, AMERICAN COLLEGE OF ALLERGISTS, 2141 Fourteenth St., Boulder, CO 80302, (303) 447-8111.

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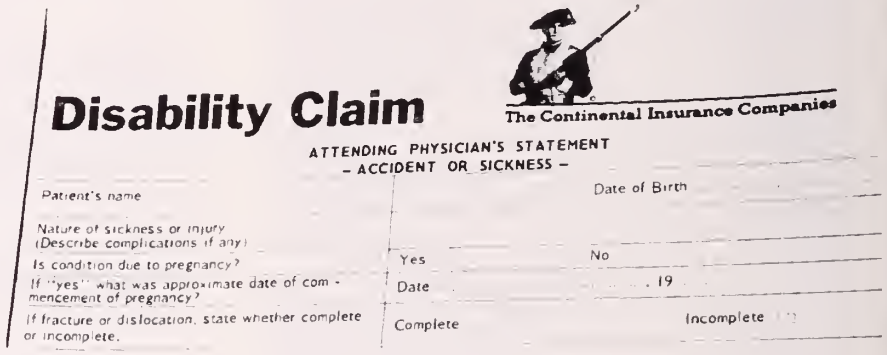

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The Journal
of the
Maine Medical Association

Volume Sixty-nine | Brunswick, Maine, March 1978 | Number 3

The Operative Treatment of Scoliosis

PAUL M. BEEGEL, M.D. and VICTOR M. PARISIEN, M.D.

This is a report on the results of the operative treatment of scoliosis at Central Maine Medical Center. The results of nonoperative treatment with the Milwaukee Brace and exercises have been reported previously in this journal.

Twenty-five patients have been followed for at least six months and are reported here. An additional eleven have had surgery too recently to qualify for review at this time.

The indications for surgery were:

1. progression of curve despite Milwaukee Brace treatment.
2. progression of curve too severe to treat with the Milwaukee Brace.
3. patients refusal to wear the brace.
4. pain severe enough to limit activities, or continuing despite adequate conservative treatment.

All the patients had idiopathic scoliosis except one where the curve was associated with Marfan's syndrome. Two patients were males. The average age was 15.2 (range 11-18).

The treatment protocol has evolved with the passing of time and refinements of technique. The present technique is as follows:

— Distraction across the selected fusion area with the Harrington outrigger apparatus, hooks inserted in facet joint above and lamina below.
— Excision of the thoracic facet joints on the concave side with a dowel plug cutter.
— Replacement of the excised joints with autogenous plugs cut from the iliac crest.
— Excision of lumbar facet joints with osteotomes and curettes.
— Replacement of lumbar joints with blocks cut from the spinous processes.
— Excision of spinous processes and morcellization into strips. Cobb type decortication of remaining laminae.
— Osteotomy of thoracic transverse processes on the convex side.
— Replacement of Harrington outrigger with Harrington distraction rod and C clamp.
— Covering the prepared bed with autogenous cortico-cancellous and cancellous strips obtained from the iliac crest.
— Cephalosporin used intravenously immediately before surgery and for two days after surgery.
— Nursing in anterior and posterior plaster shells post op.
— Cotrel cast applied at 7-10 days post-op and immediate ambulation.
— Patient allowed up for 5 h/d for the first month with unlimited ambulation thereafter.
— Cast worn a total of 5 months.

RESULTS

The average curvature was of 40 degrees (range 17 degrees to 95 degrees) as measured by the Cobb method. The average correction obtained was 50.8% (range 14%-100%) immediately post operatively. This diminished to 47.5% correction at the final tally: an average loss of 3.3% correction.

The average operating time was 3 hours, 17 minutes. Blood replacement averaged 3.7 units. The average hospital stay was 16.5 days.

COMPLICATIONS

The surgical correction of scoliosis is recognized as high risk surgery fraught with the possibility of disaster. No permanent complications occurred. There were several serious and multiple minor problems.

There was one cardiac arrest from which the patient was resuscitated successfully without sequelae.

One cord contusion occurred with full recovery

Continued on Page 80

Malignant Pleural Mesothelioma

LOUIS FISHMAN, M.D.

Pleural mesotheliomas once considered an oddity have been encountered with increasing frequency in the past 12 years. Prior to 1951, only a handful were reported in the literature. Clagett from the Mayo Clinic reported 24 cases in 1952 which they had treated at the Clinic in the previous 20 years. Hourihane from England reported 17 mesotheliomas from the London Hospital spanning the period 1917-1962 and a larger series was reported from the Memorial Hospital in New York in 1967 consisting of 37 cases encountered from 1937-1965. Wagner, et al made a significant contribution when they reported 87 patients with mesothelioma from the Cape of Good Hope asbestos fields in South Africa in 1962. Since 1965, the literature has received increasing reports of ever enlarging series of cases even from areas not considered to be large medical centers. It is with this background that I feel that a number of cases that I have encountered in the past few years is significant. In a community of approximately 68,000, which acts as a referral center for a number of smaller communities giving a total medical population of about 100,000, I have encountered 8 cases of malignant mesothelioma, 7 of them since 1974. Asbestos exposure is considered a predisposing factor in the etiology of this disease and 6 of the cases had occupations in which exposure might be significant; 3 worked in a shipyard, 2 were plumbers and 1 worked at a U.S. Gypsum Mill for a number of years. The other 2 seemed to be in occupations not exposed to asbestos; 1 was a college professor and the other a furniture salesman. There were 7 males and 1 female. Age ranged from 41-70 years.

Clinically when patients present themselves with this disease they appear to be in good health. The complaints consist of chest pain or discomfort, exertional dyspnea and a constant hacking cough. Weight loss is not a prominent feature initially. Examination of the chest may reveal dullness on the affected side with diminished to absent breath sounds. If a pleural effusion is present and often it is massive, there may be breathlessness and a mediastinal shift with tracheal deviation to the opposite side. The chest x-ray shows a thickened pleura and/or a pleural effusion. Clubbing of the fingers is relatively rare. In a patient with peritoneal involvement, whether primary or in association with a pleural lesion, ascites and gastrointestinal symptoms may be present. Peritoneal involvement however is not common. In those cases with pleural effusion, the fluid obtained on thoracentesis is straw colored in about 50%. In the remainder, it is serosanguinous to markedly sanguinous in character. Pap smears and cell blocks of the fluid are often non-revealing. Pleural needle biopsy has been disappointing in the vast majority of the cases and thoracotomy consequently has been the final diagnostic procedure. In only one case which I saw was node biopsy helpful and in fact was diagnostic.

Histologically mesotheliomas are characteristically pleomorphic in that they appear to be derived from both epithelial and connective tissue cells. There are two major types. The more common variety is the epithelial type in which there are cuboidal or polyhedral cells producing a tubulopapillary appearance or a solid group of cells without a clear tubular formation. The other variety is the mesenchymal or fibrous type in which spindle cells are arranged in an almost fascicular pattern without a stroma of abundant hyaline collagen. A mixed type is often seen.

Therapy is discouraging for long term prognosis. The findings on thoracotomy are usually that of a markedly thickened pleura involving the parietal pleura and usually the visceral pleura as well. In most cases, there is a significant pleural effusion. Except in localized disease, a curative resection is impossible. At surgery as much of the thickened pleura as possible is removed and the lung is decorticated. This may cause adherence of the lung to the chest wall, thus obliterating the pleural space and preventing the disturbing reaccumulation of a pleural effusion. Pleuropneumonectomy has been reported. It is a formidable procedure and offers little hope of cure, but Butchert, et al reported 2 cases that lived 3 and one-half and 6 years respectively after operation out of 29 cases done with a hospital mortality of 31%. None of their cases that contained mesenchymal elements survived over 2 years. They recommend that only epithelial mesotheliomas stage 1 in patients under 60 years of age be considered for this procedure. Radiotherapy offers little since these tumors do not appear to be radiosensitive. Chemotherapy on the other hand offers a palliative response in some patients. Adriomycin alone or a COMF regimen (Cytoxan®, Vincristine, Methotrexate and 5-FU) has been used. Adriomycin is given at a dose of 50 mgm/m^2 IV through a running infusion every 3 weeks. Prior to treatment, complete blood count, platelet count and EKG are performed. For responders, Adriomycin treatment is continued until a total dose of 500 mgm/m^2 is reached. The COMF regimen consists of a 5-day course of treatment administered through a running IV infusion as follows: Cytoxan 300 mgm on day 1 and day 5; Vincristine .025 mgm/Kg on day 2 and day 5; Methotrexate 0.5 mgm/Kg on day 1 and 4; 5-FU 10 mgm/Kg on days 1 through 5. The cycle is repeated every 4 weeks. Adjustments are made according to clinical and patient response. CBC, platelet count, BUN, creatinine, uric acid and liver

enzymes determinations are taken prior to each cycle.

Of the 8 cases being reported here, all had thoracotomies after other procedures consisting of thoracenteses, needle biopsy of the pleura, bronchoscopy and in one case scalene node biopsy were done. Bronchoscopy was negative in all the cases. One case had no pleural fluid, but the other seven had at least one thoracentesis. Three of these showed suspicious cells on Pap smear. Of two patients who had pleural needle biopsies, one was questioned as to the possibility of a mesothelial sarcoma. The scalene node biopsy on the one patient that had a palpable node was positive for mesothelioma. Pleurectomy and decortication of the lung was done in 7 cases; however, in each of these the resections were incomplete because of the extent of the disease. The eighth case which was first seen in 1972 was different from the others. He presented himself with an enlarged cervical node. A chest x-ray revealed some pleural fluid on the right. The first impression was that he had a lymphoma and an excision biopsy of the node was done. The node itself once removed had a cystic appearance with trabeculations. Histologically this proved to be metastatic mesothelioma. A thoracotomy was done on this patient. The pleura was thin, but had a slight granular feel. There was a mediastinal node and a hilar node present similar to the one removed from the neck. The pleural fluid was straw colored. The nodes were resected, the fluid was aspirated and a pleural biopsy taken. All showed mesothelioma. Several months postoperatively the pleural effusion recurred. After several thoracenteses, a suggestion was made to the patient that he have a pleurectomy done for palliation in order to prevent further accumulations of fluid. He requested a second opinion and arrangements were made for him at the Memorial Hospital in New York. Their recommendation was the same and a pleurectomy was done. This was complicated by excessive bleeding probably secondary to D.I.C. (19 pints of blood was used). This was successfully treated. Three weeks later he returned home. A week after this, he showed up with an empyema. It was drained. The culture grew Klebsiella. He has done well since except for the reappearance of an enlarged cervical node in 1976. This was removed and although this also showed metastatic mesothelioma, he continues to do well without any further treatment. This patient apparently has a good immunological response to his tumor.

Results

Of the eight cases, six have died, one is alive at nine months but showing evidence of increasing shortness of breath and one is alive for seventy-one months and doing fairly well. None of the patients received radiotherapy. Of those that died, 5 received some form of chemotherapy and they lived 1½-18 months. One patient received no chemotherapy and she died within 3 months from pulmonary emboli. The other two patients who are still alive are functioning. One is receiving chemotherapy 9 months since the discovery of his tumor and the other has gone 71 months without chemotherapy and still going strong.

In summary, it can be said that malignant mesothelioma appears to be increasing in frequency, asbestos exposure is an etiological factor and the condition is almost uniformly fatal.

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185 Webster St., Lewiston, Maine 04240

Sleep Apnea Treated by Intestinal Bypass

JAMES A. HOFFMEISTER, M.D., OSCAR CABATINGAN, M.D. and ANDREW MCKEE, M.D.*

A clinical picture of obesity associated with sleep disturbance, a short, thick neck, large jaws, daytime somnolence and loud snoring suggests sleep apnea syndrome. Therapeutic modalities have included diet, medication, and surgery to correct upper airway obstruction. We report a case of a morbidly obese subject who presented with a clinical picture suggesting the syndrome of sleep apnea.

CASE PRESENTATION

CP is a 34-year-old white male admitted to the Central Maine Medical Center Medical Service on February 14, 1977 with a chief complaint of difficulty in breathing. He had been a heavy snorer for at least 15 years and had been bothered by chronic nasal congestion and bilateral serous otitis media for several years. For the past 18 months, he had had difficulty sleeping. He stated that he could sleep for approximately one hour and then he had to get up and walk or sit on the side of the bed because of dyspnea. He found sitting in a chair offered his best position for sleep. In addition, he complained of falling asleep during the day while driving his automobile. This indirectly had caused the loss of his job as a traveling salesman since he could not stay awake while driving. His symptoms had worsened during the past two weeks prior to admission. His wife described his sleep pattern as one of falling asleep rapidly with immediate onset of snoring. Ventilation then became increasingly difficult followed by the patient's suddenly awakening in 10-15 minutes with moderate dyspnea. Work-up on that admission revealed a weight of 358¾ pounds with a height of 5'10". Laboratory studies revealed a normal complete blood count, urinalysis, chest x-ray, electrocardiogram, and skull x-rays. Arterial blood gases on room air revealed a paO_2 of 61.2, $paCO_2$ of 43.3, pH of 7.36. Pulmonary function studies revealed a very mild restrictive disease. The patient was then placed on a 1000 calorie reducing diet and an appointment with an otolaryngologist was made as an outpatient and he was discharged on 2-16-77.

He then returned to Central Maine Medical Center on 4-26-77 for an evaluation of possible intestinal bypass. On that admission, his weight was 382 pounds. This represented a 24 pound weight gain in the preceding nine weeks. He had marked increase in symptoms especially nasal obstruction, disturbed sleep pattern, and increased upper airway stridor. He stated that he could not remember the last complete night sleep. On this admission, he was seen in consultation by an otolaryngologist and no definite airway obstruction was noted, however, it was noted that the entire nasopharynx was somewhat obstructed due to a huge tongue and a thick, obese neck. Work-up was begun for an intestinal bypass. Complete blood count, urinalysis, electrocardiogram, chest x-ray, and chemical profile were within normal limits. Intravenous pyelogram, gallbladder series, and x-rays of the soft tissue of the neck were within normal limits. Twenty-four hour urinary 17 hydroxy-corticosteroids were slightly elevated. Twenty-four hour urinary ketogenic steroids were within normal limits. Serum cortisol levels done at 8:00 a.m. and 4:00 p.m. were within normal limits but lacked a normal diurnal rhythm. Thyroid function studies were normal. Arterial blood gases on room air revealed a pH of 7.406, paO_2 of 62, and $paCO_2$ of 36. Pulmonary function studies were interpreted as being within normal limits. Psychiatric consult revealed mild, mixed anxiety and depressive syndromes. Glucose tolerance test showed a diabetic curve. A percutaneous needle liver biopsy was performed which showed fatty infiltration of the liver. The patient was then taken to surgery on 5-2-77 with the preoperative diagnosis of sleep apnea secondary to morbid obesity. Jejunoileostomy was performed in an end-to-end fashion utilizing 12" of jejunum and 8" of ileum. An ileosigmoidostomy was then performed to decompress the blind loop. An incidental appendectomy was also performed. The patient had an uneventful postoperative recovery. He was maintained on respiratory assistance for 12 hours and was placed on low dose heparin in the post-operative period. He was discharged on 5-11-77 on calcium carbonate tablets, diphenoxylate HCL (Lomotil®), allopurinol, and multi vitamins. In addition, he was placed on a low fat, low carbohydrate, high protein, and low oxylate diet in six feedings. Discharge weight was 357 pounds. He was readmitted on 5-13-77 with a moderately severe case of bypass enteropathy characterized by nocturnal diarrhea and foul smelling flatus and bowel movements. He also suffered from acute psychological depression. He was treated with intravenous fluids for 12 hours and metronidazole (Flagyl®) by mouth. His symptoms resolved within 24 hours and he was discharged several days later. On 5-27-77, he was admitted with a mild thrombophlebitis of the left leg, and was treated with appropriate anticoagulants. On that admission, he denied any symptoms of sleep problems and he no longer snored and had no daytime somnolence. He had lost 58 pounds since the day of surgery. The first six months post-operatively revealed no further complications. He exhibited no signs of alopecia, arthalgia, renal stones, biliary stones, electrolyte abnormalities, intractable diarrhea, or disturbed sleep pattern. The patient at six month check-up was taking one diphenoxylate HCL (Lomotil) tablet a day and having four to six semisolid bowel movements per day. He was readmitted at six months post-operatively after having lost 148 pounds. Liver biopsy done on that admission revealed a marked fatty metamorphosis of the liver but not fibrosis. Other studies were within normal limits except for mild elevation of the liver enzymes.

DISCUSSION

Certain obese subjects who have a short neck and/or large jaws may develop intermittent upper airway obstruction during sleep. Typically, these subjects are observed to have periodic loud snoring and restless night-time sleep with frequent waking. The latter is usually preceded by a choking or a suffocating sensation. Guilleminault and others have recorded as many as 351 episodes of sleep apnea in an eight hour recording in a single patient with a range of 158-629 episodes. The resulting chronic sleep deprivation is believed to lead to a host of symptoms and signs including personality disturbance, excessive daytime somnolence, intellectual deterioration, and sexual problems. Additionally, hypertension, abnormal emotional outbursts, morning headaches, hypnagogic hallucination, and nocturnal enuresis have been reported to result from this condition. Eventually repeated hypoxemia, hypercapnea and acidosis during sleep is believed to lead to secondary erythrocytosis and right ventricular failure. These findings combined

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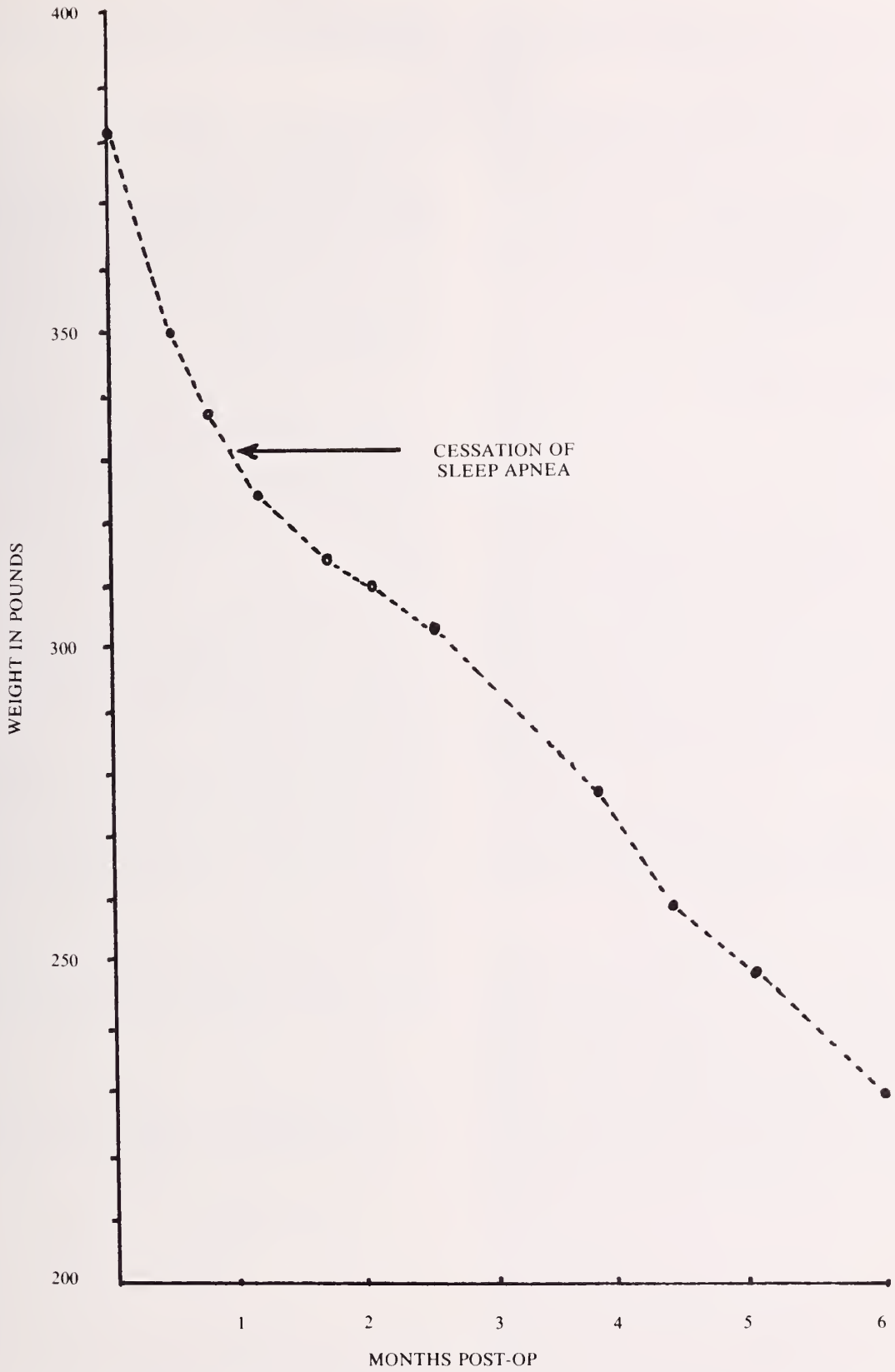

with obesity and hypersomnolence complete the picture of Pickwickian syndrome. Clinical improvement following tracheostomy or insertion of nasopharyngeal airway suggests that upper airway obstruction may be produced by mechanical factors such as backward movement of the tongue and hypotonia of the floor of the mouth. Enlarged tonsils and adenoids and unusually thick or long soft

palate have also been implicated. A central mechanism has been postulated in view of the fact that both mixed and pure obstructive sleep apnea are observed in these patients.

Therapy for sleep apnea has proved to be a most difficult problem. Weight reduction by dietary manipulation has proved to be effective; however, long term weight reduction in massively obese patients is notoriously fraught with failure and symptoms return as weight is regained.

The use of medications such as appetite suppressants, aminophylline or progestrone are unsuccessful for long-term therapy.

Surgical intervention has proved to be the most effective and most permanent form of management. When indicated, tonsillectomy and adenoidectomy may be curative. Permanent tracheostomy with a Tucker tracheotomy tube may be indicated in selected patients. Gastric bypass for control of obesity should be applicable to this problem. However, this procedure has yet to become widely used due to its technical difficulty. Intestinal bypass effectively and permanently reduces the patient's weight thus producing improvement in upper airway function. Approximately 10 percent of patients undergoing intestinal bypass have either Pickwickian syndrome or another form of obesity related ventilatory problem such as sleep apnea. Long term complications specifically related to intestinal bypass are well documented in the literature and include renal oxalate stones (0-23%), cholelithiasis (9%), polyarthralgia (0-15%), bypass enteropathy (0-25%), failure to lose weight, psychological depression, alopecia (10%), osteoporosis, and both reversible and irreversible liver failure (3-6%). Early post-operative diarrhea may be controlled successfully with dietary manipulation and appropriate drugs.

Conclusion

The diagnosis of sleep apnea in an obese patient can be made with a careful clinical history and observation of the patient's disturbed sleep pattern. Evaluation of arterial blood gases and pulmonary function studies may not be particularly helpful. Treatment primarily is surgical and may include tonsillectomy and adenoidectomy, tracheostomy with Tucker tracheotomy tube, or intestinal bypass. Intestinal bypass can be done safely in these patients and with careful follow-up, post-operative complications can be identified and treated successfully.

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Tubal Sterilization

A Review

K. C. LEONG, M.D., F.A.C.O.G.

"It is better for all the world if, instead of waiting to execute degenerate offspring for crime or to let them starve for their imbecility, society can prevent those who are manifestly unfit from continuing their kind. The principle that sustains compulsory vaccination is broad enough to cover cutting the fallopian tubes."
Oliver Wendall Holmes

The above quotation prompted this article.

Sterilization of the female has been of interest to the medical profession since Hippocrates first proposed it as a means of avoiding perpetuation of insanity through heredity. In the fourth century B.C., Hippocrates also observed that fat women appeared to bear fewer children than lean women, and he proposed that fatness should be encouraged in women who wished to remain sterile. Oligo-ovulation in obese women has long since been confirmed.

Over 100 surgical techniques for sterilization of women have been described to date. The first recorded tubal sterilization operation was carried out by Lungren in 1880 following a second cesarean section. The ingenuity of some of the described procedures cannot be denied. One of the more bizarre procedures involves the creation of a blind vaginal pouch for coitus leaving another one for pregnancy (Haendly, 1925).

No method of contraception in which frequency of use varies as much from country to country as that of surgical sterilization. On the one hand, India has depended heavily on this method, and on the other hand, in many countries, like Egypt and Indonesia, religious teaching or cultural values cause the technique to be regarded with special abhorrence.

Indications for surgical sterilization

1) Medical — Chronic constitutional disease; predictable obstetrical complications; psychiatric indications.
2) Genetic — Voluntary sterilization; compulsory sterilization on eugenic grounds.
3) Socioeconomic — Limited family income; desired family size achieved.
4) Demographic — National objective to reduce growth rate.

Public opinion and natural laws are currently in a state of transition. In most countries a lack of definite rules leaves sterilization decisions pretty much in the hands of the physician and patient.

India, where more than one million surgical sterilizations are performed annually, has had the most experience. The clear trend of the new laws adopted in many countries and the continued practice of voluntary sterilization in others now makes it clear that the procedure is accepted in a large part of the world and that it becomes difficult to continue to argue that sterilization is against "good morals."

Country	*Average Completed Family Size at Time of Sterilization*
India	5.5
Japan	2.0
Pakistan	6.9
Puerto Rico	4.7
U.S.	3.3

Indications for sterilization cannot be defined exactly. Each case must be judged on its merits. It must be borne in mind that, with present techniques, female (versus male) sterilization is more costly, more time consuming, and carries a slightly greater surgical risk. As outpatient procedures are developed and refined, costs should diminish.

At Central Maine Medical Center, 9 percent of the daily scheduled operative procedures involve tubal sterilization.

Timing of the operation

Interval sterilization — Done at convenience of patient and physician; all patients should utilize effective contraceptive measures up to the completion of the operative procedure. A percentage of post operative "failures" are luteal phase pregnancies.

Postpartum sterilization — Best done in first 24 hours after delivery; not done later than 48 hours as bacteria in uterus by this time are likely to cause a febrile postoperative course. If there has been premature rupture of membranes, intrapartum fever, manual removal of the placenta, or any factor predisposing to infection and postoperative complications, the procedure should be deferred until involution is completed. The advantages of early puerperal sterilization are easy access of the uterus and the convenience of combining postpartum and postoperative convalescence with minimal additional hospitalization.

Sterilization accompanying cesarean section is a common and convenient time to do the procedure when section is needed. However, the sterilization should not be used as an indication for cesarean section. In vaginal delivery with tubal ligation a morbidity of 3 percent but in cesarean section and tubal ligation a morbidity of 8.9 percent is experienced. Hence, section carries considerably greater risk of hemorrhage, shock, and postoperative com-

plications than does vaginal delivery followed by puerperal tubal ligation.

At the time of other pelvic surgery — In conjunction with vaginal plastic repairs, removal of ovarian cysts, hysterotomy and uterine curettage for pregnancy terminations. These opportunities for settling problems of contraception should be discussed with the patient.

Route to the surgical field

— Abdominal (laparotomy, laparoscopy)

— Vaginal (culdotomy, culdoscopy)

The decision often depends on the skill and special training of the individual operator but there are some particular points to be considered for each method.

In our institution, over a recent six month period, there were 603 gynecologic admissions. Thirty-one and seven-tenths percent of these were admitted for sterilization.

A breakdown by route to the surgical field

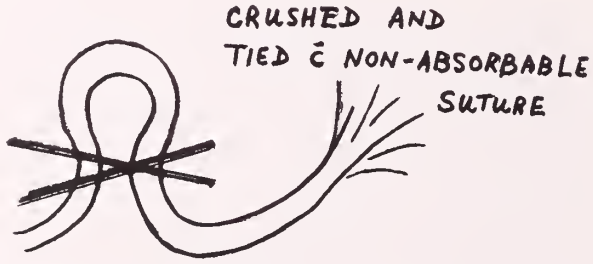
— Abdominal: laparotomy 66 (45 of which were postpartum sterilizations), laparoscopy 68

— Vaginal 57

Techniques of operations on the Fallopian Tube

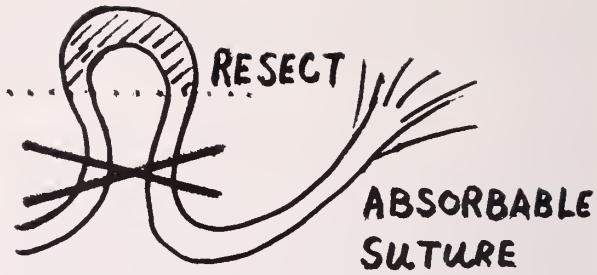
All the commonly performed procedures for surgical sterilization of the female are based on the principle of section and resection of the Fallopian tube.

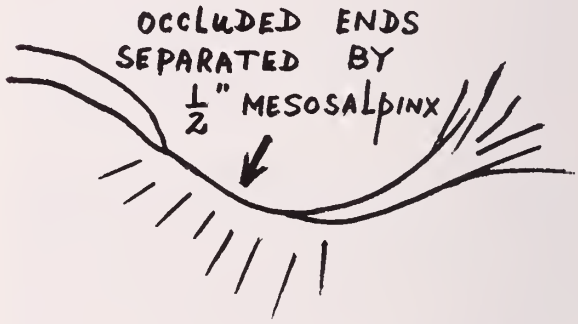
a) Madlener technique — A loop of tube is picked up with forceps and a crushing clamp placed across both limbs of the loop. A nonabsorbable suture is then tied over the crushed area. In a modification of this technique, the intervening segment may be resected. Failure rate 3.5 percent. Becoming less popular.

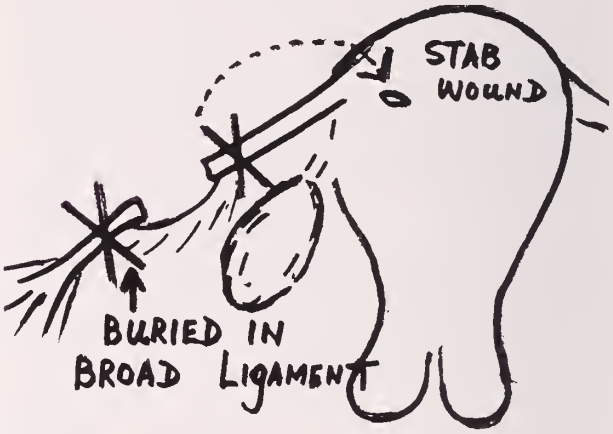


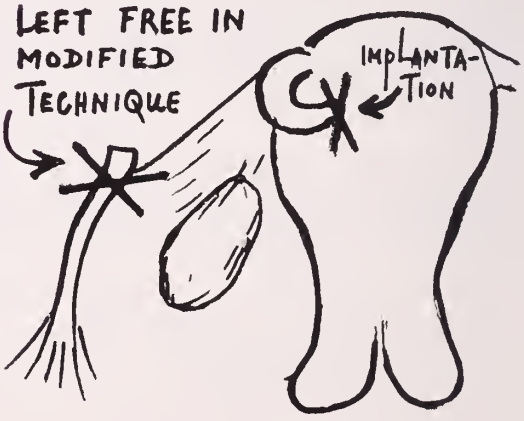
b) Pomeroy technique — Differs from the Madlener technique only in that a plain catgut ligature is tied about the two limbs of the loop without prior crushing. The intervening segment is then resected. Failure rate 2 percent with cesarean section; 0.3 percent in postpartum tubal ligation by same method.

c) Irving technique — Devised to provide further protection against the reopening of the proximal segment. This method separates the proximal and distal segments of the transected tube by burying the proximal part through a surgically created myometrial tunnel on the anterior or posterior wall of the uterus and anchoring it there. No failure as yet.









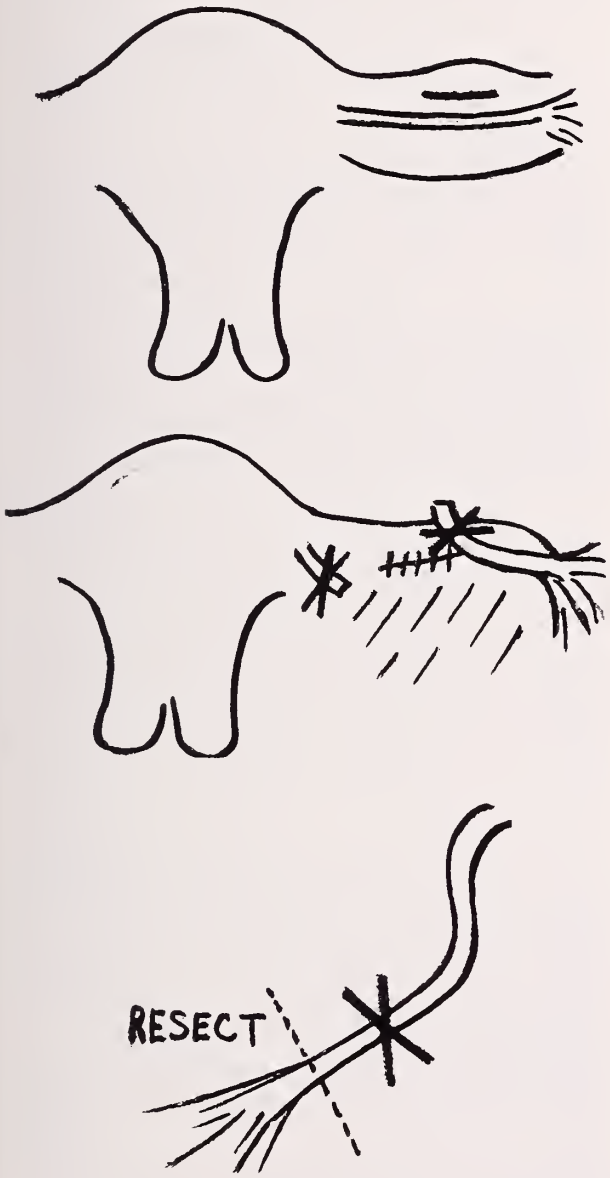
The modified Irving technique has a very high success rate and is our procedure of choice accompanying cesarean sections particularly, even though it may be associated with somewhat more bleeding. It is preferred in puerperal and interval ligation as

well unless there is some obstacle to its ready accomplishment.

d) Uchida technique — Elegant technique, possibly most complex. It is performed through a one cm. suprapubic incision. The uterine fundus may be maneuvered forward by a large curette in the uterine cavity.

1) Subserosal injection with saline-epinephrine solution.
2) Incision of mesosalpinx.
3) Excision of muscular tube; ligation with nonabsorbable suture.
4) Distal end of tube "purse-stringed."

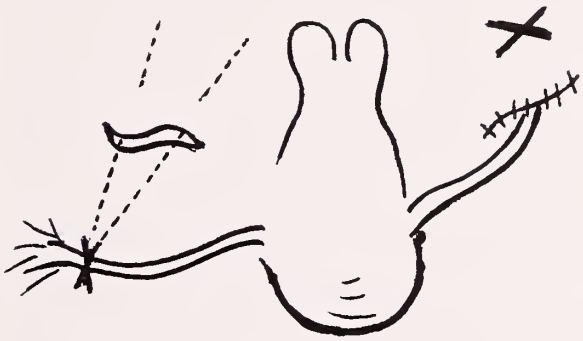
No known failure.



e) Fimbriectomy — Its simplicity, especially by colpotomy approach, is an apparent asset. It is important that the ligation be done with silk. Pregnancies (failure rate 2.3 percent) occur through a very small fistula into the short ampulla. While the fimbriae simply must have an important function of oocyte capture and transport, it is clear they are dispensable.

Temporary procedures

Several surgical techniques have been attempted, with the hope of reversibility. These usually depend on placing the fimbrial end of the tube within a surgically created space beneath the peritoneum (Aldridge operation).



Traction sutures are then placed on the end of the tube which is then drawn into the incision made in the broad ligament and the end of the tube is buried. The extent of reversibility of this procedure is yet to be determined. Pregnancies have occurred resulting from failure of the anchoring suture and the retraction of the fimbria into the exposed portion within the peritoneum.

Special procedures

a) Laparoscopy — Choice of anesthetic is controversial. One must consider the physiological consequences of the Trendelenberg position and the artificial pneumoperitoneum. Cardiovascular effects of the Trendelenberg position stem from the vascular engorgement of the head and neck, and, perhaps, decreased renal perfusion. The weight of the abdominal viscera on the diaphragm causes a decrease in the vital capacity, affecting ventilation-perfusion relationships. Elevation of the diaphragm is exaggerated when the pneumoperitoneum is induced. Expiratory reserve, residual lung volume, and, possibly, tidal volume all decrease. Unless the patient can maintain increased ventilatory efforts, these changes will lead to hypercapnia and hypoxemia.

Carbon dioxide is most frequently used for creating the pneumoperitoneum because it is non-explosive, non-combustible, and quite soluble in blood. The high solubility is advantageous because it means that only transient effects would follow accidental embolism. It was once thought that the frequently seen cardiac dysrhythmias were a consequence of CO_2 absorption. It is now known that these dysrhythmias are due to alveolar hypoventilation in the spontaneously breathing or inadequately ventilated patient. These effects can be reduced by

using a minimal amount of carbon dioxide and reducing the degree of Trendelenberg.

The creation of a satisfactory pneumoperitoneum is the keystone to any successful laparoscopic procedure. A Veress needle should be utilized to insufflate the peritoneal cavity. The needle, and subsequent laparoscope placement, should be at the midpoint of the inferior aspect of the umbilical rim. Once the abdominal wall has been distended with 3-4 liters of carbon dioxide, the Veress needle is removed, the transverse umbilical incision is widened slightly, and the laparoscope trocar inserted in a Z-type tract to avoid subsequent omental herniation.

The Fallopian tube is picked up with the grasping forceps near the cornual end and held away from surrounding structures. The current is then applied. After electrocoagulation, the tube is transected. The procedure is repeated on the other side.

An alternate method of laparoscopic surgical sterilization is by the application of a non tissue-reactive silicone rubber ring (Falope ring), a method clinically available since about 1973. This band technique is preferred by surgeons because of freedom from fear of fulguration of the bowel. The ring is 2.2 mm. thick with an inner diameter of 1 mm. and an outer diameter of 3.6 mm. The patients do seem to experience some lower abdominal and back discomfort 24 to 48 hours after application of the bands, due presumably to ischemia of the tube. The addition of 4 percent xylocaine applied to the tubes greatly reduces the discomfort of banding at first, but the effect is not lasting.

The fallopian tubes may be thickened during the midtrimester if a combined procedure of abortion and sterilization is planned. Thickened tubes may also be due to inflammation, past or present. This increases, in the author's experience, the risk of transection of the tube by the grasping forceps. Hemostasis and tubal occlusion can be achieved by application of a ring, each at the proximal and distal end of the transected tube. Electrocoagulation may be required. While grasping the selected segment, care should be taken to avoid tears of the mesosalpinx by the grasping forceps, resulting in hemorrhage which can be serious.

Time in hospital is seldom more than 48 hours, and can be reduced if necessary, especially admitted via "Day Hospital." The latter arrangement has many advantages, especially economic, in this day of the continuing rise of hospital costs.

Failure rate, one to two per thousand, is due apparently to tuboperitoneal fistulas at the point of coagulation. With experience, failure rates undoubtedly fall, but it is certainly naive to guarantee perfection to any one patient, no matter the experience of the surgeon.

Surgical errors are not included in the 0.1 percent pregnancy rate attributable to laparoscopic tubal sterilization. Coagulating or transecting the round ligament or some other structure must be considered an operative error and not a failure of properly performed laparoscopic sterilization. Only a pregnancy resulting from tubal recanalization or a spontaneous tuboperitoneal fistula of the proximal tubal stump can be looked upon as a true failure of laparoscopic tubal sterilization.

Controversies:

— Inpatient versus outpatient.
— Local versus general anesthetic.
— Carbon dioxide versus nitrous oxide for creating a pneumoperitoneum.
— One incision versus two incisions.
— Fulguration versus fulguration and transection.
— Tubal biopsy versus tubal transection without biopsy.
— Postpartum and postabortal laparoscopic sterilization.
— Physician preparation and training.

b) Colpotomy and culdoscopy — A posterior colpotomy is made to locate each Fallopian tube by touch and to draw it manually into the vagina. Alternately, a culdoscope may be used to locate and grasp the tubes. They may then be electrocoagulated intraperitoneally or brought down into the vagina. With the tubes in the vagina, occlusion is carried out by a standard Pomeroy type of tubal ligation, fimbriectomy, by electrocoagulation, or by the application of metal clips or Yoon rings.

Colpotomy tubal ligation has a relatively standard postoperative complication rate of around 5 percent. In a Mexican report of 1305 cases, there were 8 subsequent pregnancies, 15 hematomas, 6 abscesses, and 1 perforation of the rectum.

Despite these problems, the transvaginal approach to the Fallopian tubes remains a rapid, relatively simple sterilization operation in which complications can be reduced by thorough, meticulous procedures. Because of absence of an abdominal incision, the vaginal approach is more acceptable to some patients.

c) "Mini-laparotomy" — Postpartum tubal ligation can be done through a very small lower midline incision, made easy by the separation of the rectus muscles incidental to the recent pregnancy and further by the anterior position of the adnexa attached to the still enlarged uterus. The author has noticed similar small transverse or elliptical (Sauter) periumbilical incision done by his colleagues.

If sterilization in the nonpuerperal woman is done through a short abdominal incision (one inch), the tubes can be brought to an anterior position by a uterine manipulator inserted from below into the uterine cavity. This method has the great advantage of simplicity and does not require special and expensive instruments. Favorable reports on the use of the technique have come from the Far East and elsewhere.

d) Transcervical sterilization — In order to bring

absolute safety and simplicity to female sterilization, penetration of the abdominal cavity must be avoided. Laparoscopy is a sophisticated endoscopic technique, but, as an instrument for tubal sterilization, it is not the final answer. The transuterine approach to the fallopian tubes may be the ultimate solution, but, at the moment, it represents a good idea in reach of the right technique.

Sheaves of Singapore used electrocautery to close the uterotubal junction, applied by means of an instrument passed through the cervical canal. Interest in these methods has recently been revived with the use of chemicals (chemosterilization) instead of hot cautery. Silastic is a nonreactive plastic material which causes obstruction. Silver nitrate, zinc chloride or methyl cyanoacrylate in appropriate media may also be effective.

Quinacrine causes fibrosis, and holds great promise. Quinacrine studies in Chile indicate that two instillations are required in order to obtain a 90 percent tubal obstruction rate. Despite the simplicity, speed and lack of complications associated with quinacrine sterilization, a patency rate of 10 percent is unacceptable. However, technique refinements may improve results.

Research on these techniques is being actively pursued. With the perfection of the instruments for uterine endoscopy (hysteroscopy), and the identification of the ideal fibrosing agent, these nonsurgical methods promise to become practical. When this occurs, a most important new technique for fertility control will be available.

Hysterectomy as a sterilization procedure

There has been an increasing trend toward hysterectomy for sterilization. Proponents of "hysterilization" argue that when a woman desires no more pregnancies, the uterus is useless and only serves as a potential site for future uterine disease. Following tubal ligation, subsequent gynecologic disorders may be quite frequent, necessitating further pelvic surgery 25 percent of the time, and hysterectomy could make up 50 percent of these operations.

Opponents of "hysterilization" point to the high costs and risks of this procedure. Hysterectomy is associated with greater morbidity and mortality than other forms of sterilization. In one study morbidity was 22 percent for hysterectomy, and only 1 to 2 percent for laparoscopic sterilization. Hysterectomy is a drastic sterilization procedure and some women (or their husbands) are psychologically disturbed by the loss of uterus and menstrual function.

Probably the middle ground controversy is the wisest position. One concludes that hysterectomy may be desirable if there are medical indications such as dysmenorrhea, abnormal bleeding, abnormalities of the cervix, prolapse, failed tubal ligation, etc., which give justifiable rationale for the procedure.

Complications of female sterilization

Operations confined to the fallopian tubes do not have a direct effect on female physiology.

The risk of death from the abdominal operation has been estimated at one per three thousand, less than for childbirth in most parts of the world.

The overall failure rate is less than one percent, morbidity three percent and mortality rate 0.14 percent. In a consecutive study by Brenner, Bendetti, and Mishell of 100 women with the surgical diagnosis of ectopic pregnancy, 7 women were found to have prior tubal sterilization surgery. The diagnosis of ectopic pregnancy must be given careful consideration if patients conceive after a tubal sterilization procedure of any type. The diameter of the recanalized oviduct is reduced in size. Thus, the small sperm can traverse this lumen but the migration of the much larger fertilized ovum may be blocked.

Although endoscopic techniques offer a number of advantages, they also are not carried out without significant complications. Perforation of the stomach or bowel has occurred, especially in patients who have had previous abdominal surgery. As with any operation involving invasion of the peritoneal cavity, peritonitis and pelvic abscess will occur in some. Excessive bleeding from the mesosalpinx as well as damage to a major vessel, e.g., epigastric artery, have occurred requiring laparotomy. Gas embolism may occur, but this is without serious sequelae if carbon dioxide or nitrous oxide is used. Intestinal injury during laparoscopy from electrocautery and following uterine perforation during attempts to cauterize the tubal opening through the cervix have been mentioned elsewhere in this article.

In 13 follow-up studies, 78-99 percent were found completely satisfied with the operation. In 7 studies, the majority were found to have experienced no change in sexual desire or activity. Many report improved marriages and an increase in sexual drive and coital frequency (pregnancy no longer feared).

A stereotyped syndrome occurs in some women. Following sterilization, they may become overly protective of their children, complain of recurrent or constant pelvic pain, and adopt illogical but revealing attitudes about their marriage. These changes in attitude also provide the milieu for a hypothalmic basis for some of the menstrual disturbances observed following tubal operations.

Reanastamosis of the sectioned tube

Occasionally, a woman with tubal sterilization desires to recover her fertility. This change of mind may occur if an accident or illness deprives her of the children she has already borne or after a new marriage with a man who desires children of his own. Operations performed to reestablish the lumen of tubes blocked as a result of inflammatory disease have a notoriously poor record of functional success. Reanastamosis of normal tubes divided under aseptic surgical conditions give better results, with

pregnancy following the operation in 30 to 50 percent of the cases.

All reconstructive surgery performed on the oviduct is generally referred to as a "tuboplasty." A classification suggested by Margaret Moore-White is:

1) Salpingolysis — The separation of peritoneal adhesions usually secondary to an infectious perisalpingitis or endometriosis.
2) Salpingoplasty — Opening of the totally occluded distal end of the tube, as in a hydrosalpinx, either by a linear salpingostomy, removal of a wedge of tissue producing a fish-mouth eversion, or by distal resection creating a new ostium and fimbrial cuff.
3) Midsegment reconstruction — Removal of a segment of occluded oviduct due either to previous salpingitis or surgical ligation.
4) Cornual or intestitial resection and reimplantation.

Whatever new techniques are devised, the basic principle will still be that the surgeon who works on the sterile pelvis will get the best results by an operation that leaves one good tube next to one good ovary, with a minimum number of stitches. Most extensive and complicated operations for infertility are followed by extensive and complicated adhesions and defeat their purpose by changing the sterility factor from blocked tubes to tuboovarian adhesions. These can be minimized by the use of pharmacologic drugs.

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2. *Bonney's Gynecological Surgery.*
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488 Main Street, Lewiston, Maine 04240

THE OPERATIVE TREATMENT OF SCOLIOSIS — *Continued from Page 69*

after initial unilateral paresis of the lower extremity.

Two dural lacerations occurred which were repaired without sequelae.

Two pseudomonas wound infections occurred which resolved with drainage and wound care.

There were several pressure sores from casts which healed uneventfully without grafting.

Two upper hooks dislodged while the patients were ambulatory in casts. Both were removed without loss of correction.

Several cases of post op hoarseness and sore throat occurred.

Abdominal distention and cramps were the rule for a few days. All were relieved by flatus tubes, enemas or suppositories.

Several cases of urinary retention responded to intermittent catheterization.

Post op temperature elevation above 38°C was the rule for a few days. This responded to breathing exercises and was usually caused by atelectosis.

There was one minor pneumothorax which cleared without a chest tube.

In summary, the results of the surgery of scoliosis have been presented. The treatment goals were successfully achieved. A satisfactory cosmetic correction was obtained in all cases. Progression of deformity was halted in all cases. Those presenting with pain were relieved of their symptoms.

The treatment of scoliosis can be effectively and safely carried out in a moderate size community hospital as part of a treatment program that includes facilities for Milwaukee bracing, physical therapy and interested anesthesia and nursing services.

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Dr. Parisien, 416 Sabattus St., Lewiston, Maine 04240.

Medical Meeting Calendar — 1978

31st NATIONAL CONFERENCE ON RURAL HEALTH: April 5-7, Regency Hotel, Denver; sponsor, American Medical Association. Contact: American Medical Association, 535 North Dearborn St., Chicago 60610.

HYPNOSIS WORKSHOP OF THE NEW ENGLAND SOCIETY OF CLINICAL HYPNOSIS: April 13-16, South Block Building, Boston City Hospital, Boston; co-sponsor, Oral Surgery Department, Boston City Hospital, Boston. Contact: Lawrence M. Staples, D.M.D., P.O. Box 162 — U.S. Route 3, Holderness, NH 03245.

GENERAL PEDIATRICS — COURSE 9: May 11-13, Hilton Head, South Carolina; sponsor, American Academy of Pediatrics. Contact: Linda J. Nagel, Division of Education, American Academy of Pediatrics, P.O. Box 1034, Evanston, IL 60204

PHYSICIANS AND THEIR FAMILIES: June 18-23 and August 13-18, YMCA of the Rockies, Estes Park, Colorado; sponsor, The Menninger Foundation. Contact: Mrs. June Housholder, Division of Continuing Education, P.O. Box 829, Topeka, KS 66601

NATIONAL CONFERENCE ON THE CARE OF THE CHILD WITH CANCER: September 11-13, The Sheraton-Boston Hotel, Boston; sponsor, American Cancer Society. Contact: Sidney L. Arje, M.D., American Cancer Society, National Conference on the Care of the Child With Cancer, 777 Third Ave., New York, NY 10017.

Hand Decompression With Industrial Wringer Injuries

JOHN J. ROACH, M.D., FACS*

Three million four hundred seventy-six thousand five hundred and twenty tons of paper per year are produced in the state of Maine — 100,000 tons more than Wisconsin, the second largest paper producer. There are 19 paper mills, 17 pulp mills, and 7 tanneries. Their total employment is well over 20,000 people. Rollers in these industries are nowhere as forgiving as the old fashioned wringer, and injuries by them require heroic measures to get optimum recovery (Photograph 1). These injuries are some of the worst trauma short of mangling, and require continual monitoring. Contrary to most wringer injuries, these may need multiple decompressions.

Internal pressure syndromes of the whole hand, the carpal tunnel, Guyon's tunnel, and the intrinsic spaces can be seen in all combinations. The hand, a compound cylinder with thick fixed volar skin, has few escape hatches. Often the physician is saved from a catastrophic result by the wry paradox of the injury itself, which may have already provided the necessary decompression. The physician must be aware of the kaleidoscoping pathophysiology before him.[1] He should know that pressure above lymphatic and venous outflow in the strongly sheathed conical intrinsic muscle units leads to an acute "intrinsic minus hand" — the MP joints are extended and the PIP joints flexed (Left, Figure 1).[2] Only in the late contracted stage does one see the intrinsic "plus" hand with the reverse (Right, Figure 1).[2] The progression of the intrinsic compartment syndromes to irreversible Volkmann's contractures and functional loss of the hand is a catastrophe to be avoided (Left to Right, Figure 1).[2]

Other types of pressure phenomena need to be continuously evaluated also. Pressure on the median nerve and eight tendons in the carpal tunnel leads to the classical sensation loss from the carpal tunnel syndrome. A centimeter away the ulnar nerve divides with a motor branch passing around the vulnerable hook of the hamate. Pressure here means that both the carpal and Guyon's tunnel may need to be opened immediately. Motor ulnar nerve compression from a fractured hamate hook may require its excision as well.[3] Pressure within the hand as a whole may interrupt vascular arcades or digital arteries and needs to be appropriately decompressed.

Evaluation initially on an eight-hourly basis should include a continual watch for the "intrinsic minus hand" with stretch testing of each finger in abduction and adduction. Increasing pain is noted with increasing interossei compartment pressures. Electromyography of the intrinsics will note the onset of diffuse fibrillations or conduction delay as pressure damage develops. In some cases, this may be days later! Loss of distal motor function of the ulnar nerve and loss of pain with stretch testing is an ominous sign for the interossei muscles.[2] Immediate decompression of the involved intrinsic compartments should be instituted (Diagram 1).[4] Excellent clinical results can be anticipated by releasing intrinsics from their unyielding compartments prior to the onset of irreversible fibrous changes. Cyanosis, paresthesias, and lack of pulses should be carefully documented. With intrinsic compartment syndromes alone, sensation in the digits may be normal! Loss of sweating, as noted by examination of the skin pores with an ophthalmoscope, may also coincide with the onset of the need for decompression.[5] The Doppler flowmeter can be used in surgery and repeatedly thereafter to evaluate wrist and digital pulses, and can be interpreted as meaning that nutrition is adequate for several centimeters in all directions.[6] Lateral or dorsal decompressions may be all that is necessary for pulsatile losses (Photograph 2). Where primary closure is not possible, the hand can be closed with split thickness grafting (Photograph 3). The grafting should probably be delayed from 48 hours to a week, according to the wound appearance, since too hasty wound coverage will only lead to graft loss.[7] Constant elevation with stockinette and soft fluffy dressings may be needed for many weeks.[8] Some centers advocate the use of 10 milligrams of prednisolone po qd for ten days and have noticed no complications from the use of this drug.[1] Late chronic edema may be treated with intermittent compression devices.[9]

SUMMARY

Compression dressings are no longer acceptable treatment for wringer injuries. Severe cases require continual monitoring with decompression of spaces or compartments within the edematous hand as well as nonconstricting elevation. Prevention of tissue loss, sensation loss, and miniscule Volkmann's contractures can then be anticipated. Further preventive measures at the factory and possibly legislative level, to improve the safety of these machines, seem to be in order.

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1. Grant, G. H.: The "Intact" Hand after Crush and Burn.

Photograph 1
Rollers in a papermill through which the hand in photograph 3 passed, typifying those found throughout the paper and tanning industries.

Photograph 2
Lateral decompressions secondary to the injury itself — not in ideal positions, but adequate — along the radial surface of the index finger and the ulnar surface of the hypothenar eminence.

Photograph 3
Split skin graphs used as a dressing at 48 hours when a good vascular bed was obvious.

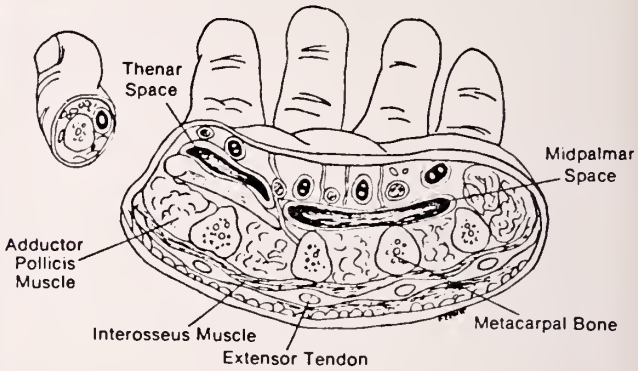

Fig 2.—Top, Cross section of interosseous space. Bottom, Incisions in dorsal fascia to decompress unyielding interossei canals.

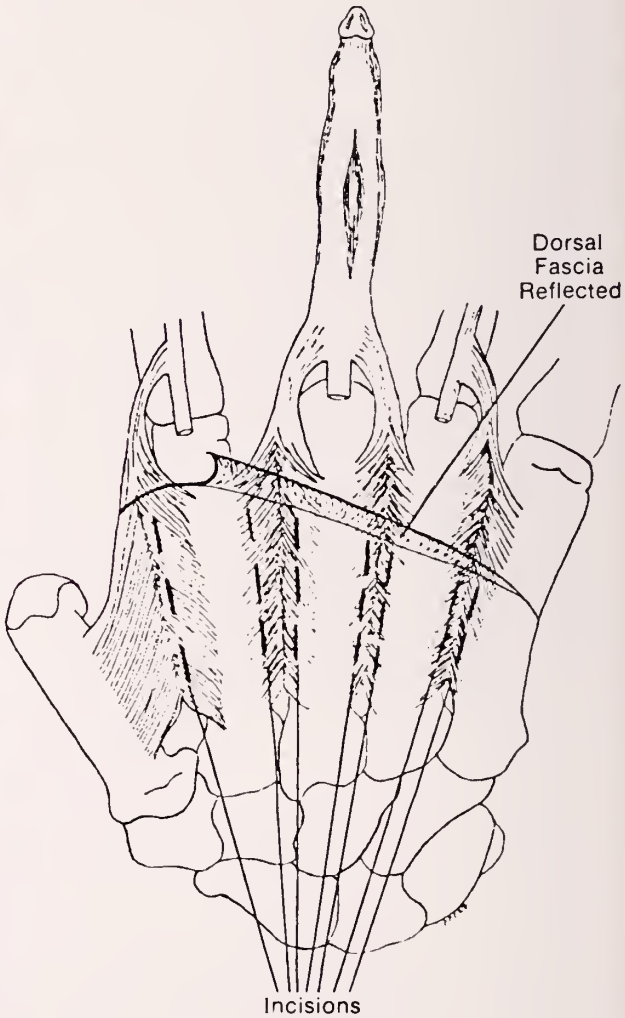

Diagram 1
Both compartments in each interdigital space can be decompressed through a single verticle dorsal incision for each interdigital space. The muscle will acutely pout and blood and serum will exit.

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Fig. 1. Left — "Intrinsic minus hand." Right — "Intrinsic plus hand."

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Surveys of Maine Hospitals: An Overview*

ALFRED HURWITZ, M.D.

As a consultant for the Hospital Services Division of the Department of Human Services, I have visited more than 40 hospitals in Maine during the past two (2) years. Since many of the deficiencies that I have discussed at my exit interviews at those hospitals are similar, I was stimulated to prepare this paper emphasizing the problem areas and to make recommendations for their correction.

Since I am primarily interested in the level of patient care, the following approach was evolved to obtain as much information as possible pertaining to that study. Several weeks in advance of my visiting the hospital, a letter is sent to the executive director requesting that the hospital's Bylaws and Rules and Regulations be sent to me. In addition, records covering a recent six-month period are to be made available in the record room upon my arrival. Those records include all deaths, all appendectomies (primary) other than acute appendicitis, all hysterectomies revealing normal uteri and including chronic cervicitis and all cholecystectomies except those revealing stones. I also review about 10 T and A records to see if indications justify the operation.

I review the Bylaws and Rules and Regulations several days in advance and make appropriate annotations which I discuss with the President of the Medical Staff and the Administrator of the hospital. The charts requested are reviewed and the case numbers and the discrepancies are recorded so that they can be discussed at my exit interview and in my final report.

Shortly after the team arrives at the hospital, we make a detailed tour with the Executive Director or his associate. The licensure survey team includes a registered nurse with a background of training in the operating room, intensive care unit and in nursing policies and education. The team leader, the Director of Hospital Licensing, is a former hospital administrator with a vast experience in hospital management. Either or both of these members revisit the hospital on a selective basis, about three months after our combined survey to determine how the hospital has dealt with our recommendations. Other members of the team who join us from time to time include a registered nurse who is Head of the Hospital Infection Control Program for Maine, a dietitian, a sanitatian and a laboratory consultant, and a representative of the State Fire Marshal's Office, and a Medicare Consultant if the hospital isn't JCAH accredited.

During the 2-4 days (depending on the size of the hospital) spent there, I meet the President of the Medical Staff, the Pathologist, the Radiologist, members of the Board of Trustees and of Administration. I also discuss the quality of the medical records, delinquent charts and rapport with physicians with the Medical Records Librarian, the coverage in the Emergency Room with the supervisor and problems pertaining to the Operating Room with its supervisor. I review the completed medical audits to determine if the criteria for the study were appropriate, what was learned from the audit, and what recommendations have been made to correct existing deficiencies.

The exit interview takes place on the last day of our hospital review when dialogue concerning our findings is encouraged. Members of the Board of Trustees, especially its officers, members of the Medical Staff and Administration are present. A second exit interview is conducted by other members of our team and the participants include members of hospital departments; e.g., nursing, pharmacy, housekeeping, maintenance, fiscal affairs, etc. The President of the Medical Staff and of the Board of Trustees are also encouraged to attend that meeting which I, too, usually attend.

At the exit interview the following subjects are usually discussed:

1. *Medical Records*

Often the records contain inadequate histories, physicals, discharge summaries, and progress notes. The failure, in general, is in the direction of omissions, e.g., incomplete description of the physical findings including rectal and vaginal examinations, skimpy discharge summaries that fail to afford the reader a concise but complete resume of the patient's course and inadequate progress notes. Concerning the latter, I encourage the employment of the word SOAP which includes a description of patient's Subjective symptoms, Objective findings, Assessment and Plan. The failure to suspend a physician because of delinquent charts is an abrogation of the Bylaws. This type of suspension should be automatic, apply to *all* physicians, and be lifted only when they have completed their charts.

2. *Committees*

Committees as outlined in the bylaws should be limited to those that can make a significant contribution to the enhancement of patient care and the more efficient administration of hospital functions. They should have enough significance to warrant their meeting regularly, at least four times a year.

Since the President of the Medical Staff selects members of all committees, except the executive committee, it behooves him to choose those people,

*This article represents my own point of view and does not necessarily reflect those of the Department of Human Services, State of Maine.

medical as well as paramedical, who by virtue of their training, interest, and experience can contribute significantly to that committee. It should be chaired by the physician who has exhibited a deep interest in that field and who will be a dynamic, productive chairman. I should like to make a plea that the agenda and the preliminary groundwork be implemented in advance to avoid "spinning one's wheels at the meeting." The aim should be to eliminate tabling of issues because information is lacking and the audience unprepared.

Rules for attendance should be as rigidly enforced as for staff meetings.

In many hospitals, the Joint Conference Committee meets haphazardly or not at all. This committee is extremely important since it represents an amalgamation of the troika — the Board of Trustees, Administration, and the Medical Staff. It should prove to be a learning experience for members of all those bodies. The trustees should be cognizant of the quality of patient care and their knowledge augmented by reviewing minutes of the Medical Staff and its standing committees, and the results of medical audits.

Utilization Review, Medical Audits, Tissue and Mortality Committees can be grouped under the heading of Medical Care Evaluation and represent the cornerstone for improving the quality of patient care. Common failures are the lack of documentation of critical discussions relating to diagnoses and treatment and absence of information concerning what was learned from the case and what recommendations were made to eliminate those problems in the future.

3. *Informed Consent*

The surgeon should impart to his patient in lay terms what he is planning to do at the operating table. This information should be complete including such possibilities as removing the appendix at the time of performing a cholecystectomy or hysterectomy or excision of a skin tumor after a major operation. He should also inform his patients about the most common complications that might ensue. The fact that they occur rarely can be emphasized in his discussion to lessen the patient's anxiety. This information should be recorded and signed by both the patient and the surgeon and also, if feasible, by a witness who can corroborate the fact that that discussion took place. It does not seem justifiable or safe to have the Informed Consent Form signed by the admitting office, a nurse, or a clerk in lieu of the surgeon.

4. *Delineation of Privileges*

Delineation of privileges range from none to the "Briggs Form" which is a complete check-off list of diseases to be treated and operations to be performed. Although this form is not foolproof, it constitutes a worthwhile attempt to pinpoint the physician's limitations as well as his capabilities. The recurrent failure exhibited by most hospitals is the lack of evidence that all physicians' privileges are reviewed critically and failures, invariably of commission, are corrected. This type of probing review should be carried out annually and "rubber stamping" should not be condoned. The criteria employed for granting privileges should be based on the physician's training, experience, and competence (review of his results).

5. *Role of Trustees*

Today's trustee has multiple and diverse responsibilities which run the gamut of fiscal affairs, construction, salaries, fringe benefits to determination of the quality of medical care. The latter is an obligation that he has become aware of recently since he as a member of the governing body of the hospital, must be assured that no physician is performing in a substandard manner. In answer to the question "How can a trustee be apprised of the quality of medical practice in his hospital?", the following ten recommendations are made:

a. He should receive and review minutes of all committee meetings and determine who attended and who was absent, what was discussed and were differences of opinion and recommendations documented. One should assume that if it hasn't been documented, it has not been done. Is the committee meeting regularly, and is it properly constituted as stated in the Bylaws?

b. He should review narrative resumes of all medical audits which should point out the deficiencies that exist and the recommendations to eradicate them.

c. Minutes of the staff meetings should assure him that all standing committees have made their reports and most important, that there is evidence of a learning experience like discussions of unusual cases, complications, or reviews of medical literature.

d. He should review line by line, reports from JCAH and the licensure survey team and make sure that their recommendations are being effected as soon as possible.

e. Delineation of privileges should be filled out by each physician and reviewed by a medical director or in smaller hospitals, by the President of the Medical Staff. The physician may check off procedures for which he does not have adequate training, experience, or satisfactory results. In those instances, it is essential that a key physician be willing to confront that physician "eye-ball to eye-ball". Those forms should be reviewed annually prior to reappointment.

f. Informed consent should be obtained by the surgeon or physician and imply that he has discussed with the patient procedure or procedures that he contemplates performing and the risks and complications that might ensue.

g. The trustees should have tangible evidence that the physicians are employing appropriate

"checks and balances" and documenting the fact that they are carrying out meaningful peer reviews to enhance the quality of patient care. If the physicians fail to carry out this important function, then the confrontation with the offending physician should be conducted by the troika of the President of the Board of Trustees, President of the Medical Staff and the Administrator.

h. Trustees should encourage curtailing medical costs by making sure that physicians make every effort to eliminate unnecessary laboratory determinations, procedures like IPPB which are rarely indicated and unwarranted medications. Good medicine does not have to be *unduly* expensive.

i. Most communities need additional medical specialists, especially those engaged in family practice. The trustees with key physicians should leave "no stone unturned" in encouraging applicants and their wives to come to their community. The newly acquired physician should not be "hamstrung" by inappropriate limitations to practice. In general, hospitals that have failed to attract well qualified doctors during the past ten or more years should come under close scrutiny to determine the reasons.

j. All physicians and members of all departments should be expected to document the fact that they have acquired continuing education on a steady basis. To ensure that educational programs for all departments are made available in the hospital, the necessary equipment including television monitors, slide and movie projectors should be made available. A Head of Education should be selected who would be responsible for obtaining, usually on loan, the best available teaching slides, films, or cassettes and arrange to show them on schedule to members of every department in the hospital. Of course, the equipment should be employed to project newer clinical developments for the edification of all members of the Medical Staff. Failure to acquire new knowledge means going backwards.

6. *Peer Review*

The failure of many medical staffs to practice peer review in a constructive, critical manner is most discouraging and makes one wonder whether physicians are capable of policing themselves.

In "The Rift Between Medical Staffs and Hospital Boards," Betty Jane Anderson[1] made the following appropriate statements: "If the medical care of patients is to remain the primary responsibility of physicians, and not impersonal hospital corporations, then it is essential that the organized medical staff of a hospital truly function as the name implies, with emphasis on the word organized. The hospital medical staff is, and should be, more than a group of individual physicians who have some sort of relationship to the hospital and its governing board merely by virtue of the hospital privileges accorded them individually.

"The medical staff physician has an obligation to the organized medical staff — the obligation to participate productively and responsibly. Likewise, the organized medical staff has a *basic obligation to discipline its members so that together they may fulfill, through self-government and self-direction, the medical management of the hospital. If the medical staff defaults in this obligation, the governing board can be expected to react.*"

In large hospitals with full-time salaried chairmen of departments the latter are held responsible for discussing, "eye-ball to eye-ball", errors of judgement or substandard performances with members of their respective departments. In the smaller hospitals comparable to the size of most Maine hospitals, this type of confrontation rarely takes place mainly because it is an unenjoyable experience. It requires the presence of a physician, who is professionally competent, self-critical as well as critical of others and has the ability to confront his colleague concerning his malfunctions in such a way that they will not be perpetuated. It would seem worthwhile to give this all-important physician an appropriate title and also a stipend. These emoluments would contribute towards making him a persona grata in the hospital and enhance his desire and authority to review and implement the quality of care. In some hospitals, deficiencies in the practice of medicine are mentioned, but there is little evidence that attempts at correction are carried out. This latter step is an extremely important stimulus to raising the quality of medical care and constitutes a system of "checks and balances." This review should be the responsibility of the hospital staff and should not be relegated to outside agencies. If hospital staffs fail to police themselves, then intervention by other agencies will become necessary. "The fault is not in our stars, but in ourselves that we are the underlings."

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Clinical Use of Hemostatic Agents

GORDON D. O. LOWE, M.B., M.R.C.P. and DAVID H. LAWSON, M.D., F.R.C.P.

This review is concerned with preparations that are used to promote arrest of hemorrhage. Such agents can be classified as either locally or systemically acting. Local hemostatic agents are applied topically to promote clot formation in areas of capillary oozing on body surfaces and internally during surgery. They are eventually absorbed. Such agents include thrombin, gelatin sponge, oxidized cellulose, and collagen fibrils. Systemic hemostatic agents, the subject of this review, are given to correct specific generalized hemostatic deficiencies seen in a wide variety of clinical situations and include vitamin K preparations, aminocaproic acid and tranexamic acid, antihemophilic factor, fibrinogen and other blood derivatives.

NORMAL AND ABNORMAL HEMOSTASIS AND FIBRINOLYSIS

Coagulation

The sequence of events promoting hemostasis when a blood vessel is damaged may be summarized as follows: (1) The vessel contracts, affording transient hemostasis. (2) Blood platelets adhere to the edges of the damaged vessel wall and to each other; this platelet aggregate forms an initial, loose hemostatic plug. (3) At the same time the coagulation system is activated, resulting in the formation of fibrin strands which reinforce the platelet plug; this platelet-fibrin mesh-work firmly and finally seals the vessel defect. (4) The fibrinolytic system is activated, breaking down fibrin; under normal circumstances this proceeds slowly over a period of days, in parallel with tissue repair processes.

The coagulation and fibrinolytic systems are shown in greater detail in Figure 1. Fibrin is formed from circulating fibrinogen (factor I) by the enzyme thrombin. Thrombin is itself formed from a circulating plasma precursor, prothrombin (factor II) as a result of the interaction of other plasma protein coagulation factors. All coagulation factors are identified by Roman numerals in a standard international classification, and all are synthesized in the liver except factor VIII whose site of synthesis is uncertain. Prothrombin is converted to thrombin by the interaction of factor V, factor X, phospholipid (from damaged tissues or platelets) and calcium (formerly known as factor IV). This "final common pathway" of thrombin formation, and hence fibrin formation, can be activated by either of two systems — the extrinsic or intrinsic thromboplastin systems.

When blood is taken by clean venipuncture, placed in a glass tube, and incubated at 37°C, clotting normally occurs within 5 to 10 minutes (whole blood clotting time). All factors required for coagulation are present in the blood, hence this coagulation pathway is termed the *intrinsic system*. Surface contact with glass initiates interaction of factors XII and XI. Activated factor XI then activates factor IX, which interacts with factor VIII, phospholipid, and calcium to activate the final common pathway of thrombin and fibrin formation discussed above. This pathway is an amplification system; increasing amounts of activated coagulation factors are formed at each stage of the process.

The function of this intrinsic system is crudely tested by the whole blood clotting time. More reproducible tests are the partial thromboplastin time (recalcification of citrated plasma) and activated partial thromboplastin time (prior activation with kaolin surface and cephalin phospholipid). However, these screening tests may be insensitive to moderate defects of factor VIII or factor IX, and if hemophilia is suspected, then specific assays of factor VIII and factor IX should be performed.

The intrinsic system is defective, and the partial thromboplastin time prolonged, in the following disorders and therapies: (1) Congenital deficiency of factor VIII activity (hemophilia A and von Willebrand's disease) or factor IX activity (hemophilia B, also known as Christmas disease). (2) Acquired inhibitor of factor VIII, which may develop in hemophiliacs after treatment with factor VIII or arise spontaneously in otherwise normal subjects. (3) Acquired factor IX deficiency due to liver disease, vitamin K deficiency, or vitamin K antagonism by oral anticoagulants. (4) Heparin, which inhibits thrombin and factors IX, X, and XI. (5) Massive transfusion of stored blood, which is deficient in factors V and VIII. (6) Disseminated intravascular coagulation, in which factor VIII is consumed along with fibrinogen and factor V.

When tissue extract is added to fresh blood or plasma, clotting occurs rapidly — normally in about 10 to 15 seconds. The addition of this extrinsic thromboplastin (formerly known as factor III) from

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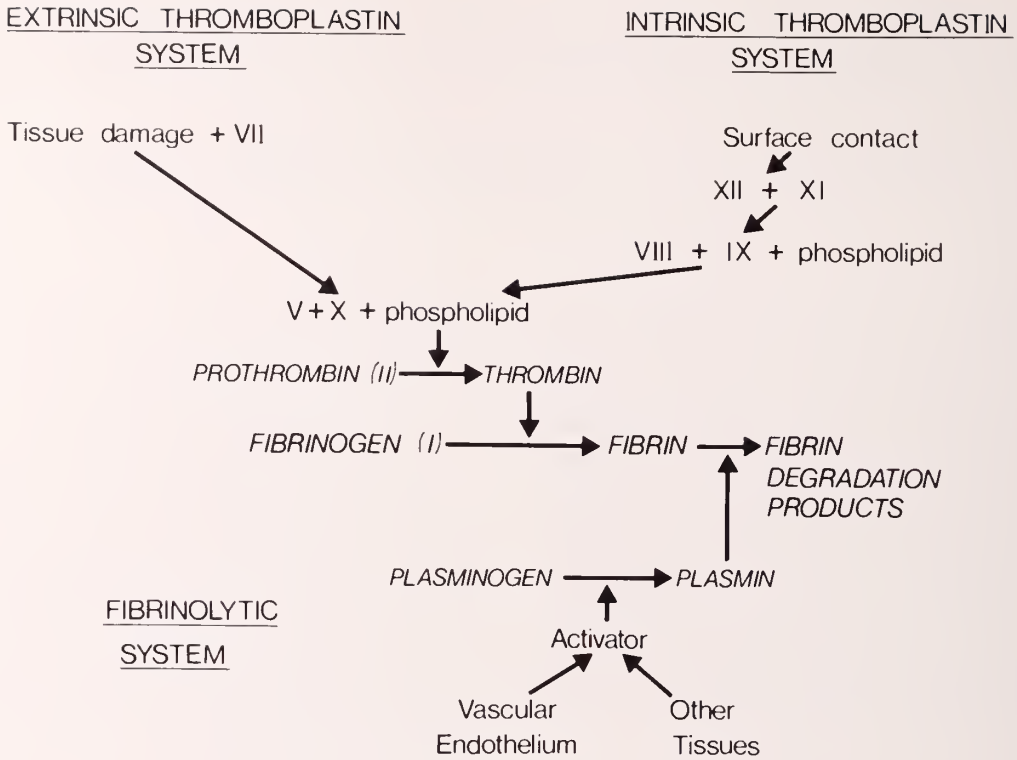

Fig. 1. Coagulation and fibrinolytic systems.

damaged tissue initiates the extrinsic thromboplastin system; the thromboplastin interacts with factor VII to activate the final common pathway of thrombin and fibrin formation. The function of this extrinsic system is tested by the prothrombin time; a standard tissue thromboplastin is added to citrated plasma which is then recalcified.

The extrinsic system is defective and the prothrombin time prolonged in the following disorders and therapies: (1) Acquired deficiency of factors II (prothrombin), VII, and X due to liver disease, vitamin K deficiency, or vitamin K antagonism by oral anticoagulants. These three factors, along with factor IX discussed above, are synthesized in adequate amounts only when liver function is reasonably intact and adequate supplies of vitamin K are available. Concentrates of factors II, VII, IX and X (prothrombin complex concentrates or factor IX concentrates) are available for the correction of such combined defects. (2) Heparin therapy, which inhibits factor X and thrombin. (3) Massive transfusion of stored blood, which is deficient in labile factor V. (4) Disseminated intravascular coagulation, in which factor V is consumed.

Fibrinolysis

The mechanisms of the fibrinolytic system are not as well understood as those of the coagulation systems. Fibrin is converted into soluble breakdown products (fibrin degradation products) by the enzyme plasmin. Plasmin can also digest fibrinogen to form similar products; such products are therefore termed fibrinogen/fibrin degradation products (FDP). Plasmin is formed from a circulating plasma precursor, plasminogen, which is incorporated into clots along with fibrin during coagulation. Activators of plasminogen are present in all body tissues, especially vascular endothelium; coagulation factor XII can also initiate fibrinolysis. FDP are anticoagulants; like heparin, they inhibit the conversion of fibrinogen to fibrin by thrombin.

In many clinical situations, bleeding may occur because of a marked deficiency of plasma fibrinogen, accompanied by increased fibrinolytic activity and high levels of anticoagulant FDP. A rapid screening test for this defibrination syndrome is the thrombin clotting time, in which thrombin is added to citrated plasma. The thrombin clotting time is prolonged with a marked deficiency of plasma fibrinogen and/or high levels of FDP. (Heparin, which also inhibits thrombin, will also prolong the thrombin time). Marked fibrinogen deficiency will also result in a small clot in clotting time tests.

The defibrination syndrome usually arises from disseminated intravascular coagulation (DIC), which may complicate a wide variety of acute illnesses and operations; a more chronic form is seen in malignant diseases, retained dead fetus, and giant hemangioma. The coagulation system is activated by release of thromboplastins from damaged tissues or by widespread damage to the endothelial lining of small blood vessels. There is secondary activation of the fibrinolytic system, which digests fibrinogen and fibrin to their degradation products. Clinical features include (1) thrombosis; (2) hemolytic anemia, due to damage to red cells by fibrin strands

in the capillaries; and (3) bleeding, due to depletion of fibrinogen, platelets, factor VIII and factor V, and to the anticoagulation action of FDP.

Less commonly, defibrination arises from primary activation of the fibrinolytic system, resulting in the conversion of fibrinogen to degradation products and consequent bleeding. Such primary pathological fibrinolysis occurs in similar situations to DIC (post partum, after surgery, and complicating malignant disease). Therapeutic activation of the fibrinolytic system, to lyse thromboemboli, may be effected with urokinase or streptokinase. Bleeding may then occur if there is excessive consumption of fibrinogen and production of degradation products.

General Management of Systemic Hemostatic Defects

Diagnosis

Accurate diagnosis is essential for proper management of generalized hemostatic defects. Frequently the defect is obvious — for example, bleeding in patients on anticoagulant therapy, patients known to be thrombocytopenic, or in known hemophiliacs. Often laboratory tests are required to provide specific diagnosis and to guide replacement therapy.

A family history of bleeding or a past history of prolonged bleeding after injury or surgery (especially after extraction of teeth, tonsillectomy, or childbirth) are commonly found in patients with congenital coagulation defects, such as the hemophilias. However, one-third of hemophiliacs give no family history, and mild hemophiliacs may appear to have normal coagulation after minor hemostatic stresses, yet may bleed profusely after major trauma or surgery. It is essential to distinguish hemophilia A (factor VIII deficiency) from the less common hemophilia B (factor IX deficiency, Christmas disease) so that the appropriate factor may be replaced; the presence of a factor VIII inhibitor will also influence therapy.

Anticoagulant and fibrinolytic therapy are usually obvious causes of defective hemostasis. Less obvious are drugs and chemicals causing thrombocytopenia, and drugs such as aspirin and dextran that produce defects in platelet function rather than quantity. Renal failure and paraproteinemias also cause functional abnormalities of platelets. Purpura with enlargement of liver, spleen or lymph nodes suggest the possibility of thrombocytopenia from reticuloendothelial neoplasia. Liver disease, obstructive jaundice, or malabsorption suggest a defect of vitamin K-dependent clotting factors. Defibrination syndromes can complicate obstetric accidents (septic abortion, antepartum hemorrhage, retained dead fetus), surgery (especially prostatic, lung, and cardiac bypass), acute hemolysis (transfusion reactions, burns, snakebite), septicemias, and malignancy. Massive transfusion of stored blood, deficient in platelets and labile coagulation factors (V, VIII), may also cause bleeding.

The pattern of bleeding differs in platelet defects and coagulation factor defects. In platelet deficiency, bleeding occurs soon after injury and may be alleviated by pressure: purpura and oozing from venipuncture sites are common. In clotting factor defects, bleeding is commonly delayed for some hours after injury and is not alleviated by pressure: large spreading subcutaneous bruises and bleeding into muscles and joints are characteristic.

Blood samples for hemostatic screening should be taken by clean venipuncture at sites distant from intravenous infusions. Samples commonly taken are an E.D.T.A. sample for blood count, blood film and platelet count, a citrated sample kept on ice for coagulation tests (thrombin time, prothrombin time, activated partial thromboplastin time), and a sample for fibrinogen/fibrin degradation products (if defibrination is suspected). Initial results should be available within an hour and will indicate whether a hemostatic defect is due to thrombocytopenia, to coagulation factor deficiency (of extrinsic, intrinsic, defibrination, or multiple type), or to both. Further tests of coagulation or fibrinolysis, or further investigation of thrombocytopenia, may then be indicated. If the hemostatic defect is due to blood vessel or platelet dysfunction, the coagulation screen will be normal.

General Management of Acute Hemorrhage

Unless intravascular volume is maintained with intravenous fluid, plasma, or blood, and shock prevented, small blood vessels can be damaged and DIC may occur, which will increase the coagulation defect. Treatment of the underlying disorder is especially important in the defibrination syndromes, and, as in cases of abruptio placentae, may be all that is required.

General Management of Chronic Hemostatic Defects

In congenital bleeding disorders, accurate diagnosis, screening of relatives for cases and carriers, and genetic counseling are most important. Patients should be educated on the risks of trauma, surgery, and tooth extraction, and provided with a card stating the type and severity of the disorder, blood group, and physician or reference center. A "physician-alert" bracelet may be valuable in case of accident. Patients should be warned not to take salicylates, which impair platelet function and exacerbate bleeding. Intramuscular injections should be avoided as large, painful, crippling hematomas may occur.

Despite the benefits of modern replacement therapy, persons with severe hemophilia commonly have problems with chronic arthropathy, education, employment, personal relationships, and drug addiction. Such patients are best managed at a hemophilia center where physicians, surgeons, hematologists, physiotherapists, social workers, and dentists communicate regularly and are aware

of optimal management of these special problems.

Systemic Hemostatic Agents

Systemic hemostatics are grouped into those that are derived from blood and those that are not. The latter group includes protamine, vitamin K preparations, and fibrinolytic inhibitors. The only use of protamine sulfate is to neutralize heparin in the event of major bleeding during heparin therapy.

Vitamin K Preparations

Vitamin K is required for the hepatic synthesis of coagulation factors II, VII, IX, and X. Vitamin K therapy may be needed in (1) bleeding due to vitamin K deficiency, and (2) bleeding during treatment with oral anticoagulant drugs. Oral anticoagulants antagonize vitamin K by competitive inhibition; consequently their effect may be reversed by vitamin K administration.

Most dietary vitamin K comes from leafy green vegetables. Another source of the vitamin is the endogenous bacterial flora of the gut. Pure dietary deficiency is rare but may occur in patients with steatorrhea who are on low fat diets and in patients on long-term parenteral nutrition. Reduction of the normal bowel flora by prolonged antibacterial therapy may reduce bacterial synthesis of vitamin K and thereby cause deficiency. However, significant vitamin K deficiency usually arises from failure of intestinal absorption. Naturally-occurring vitamin K is fat-soluble and normally is absorbed with fat; it is not absorbed when deficiencies of bile salts (as in obstructive jaundice) or pancreatic lipase (as in pancreatic insufficiency) are present. Extensive intestinal resection or disease may also produce vitamin K deficiency by reduction of jejunal fat absorption or ileal bile salt reabsorption.

"Vitamin K" is a general name for a group of napthoquinone derivatives. The commonly used vitamin K preparations are synthetic compounds. They include the fat-soluble substances phytonadione (vitamin K1) and menadione, and the water-soluble salts of menadione — menadione sodium bisulfite (Hykinone) and menadiol sodium diphosphate (Synkayvite). Phytonadione is the preferred drug since it has a more rapid and potent effect and is less toxic to neonates.

Phytonadione may be given orally, intramuscularly, and intravenously. Intravenous injections should be given slowly since adverse effects (flushing, sweating, sensation of chest constriction, cyanosis, peripheral circulatory failure) may occur. Intravenous injection is usually reserved for hemorrhage during oral anticoagulant therapy. The usual dose range is 5 to 50 mg in 24 hours. Large doses render the patient refractory to further oral anticoagulant therapy for several days.

Parenteral therapy is indicated in malabsorption states; the intramuscular route is generally used. An example is correction of hemostasis before surgery in patients with obstructive jaundice. Here, the dose of phytonadione is 10 to 20 mg daily, and the response — synthesis of vitamin K-dependent clotting factors — is assessed by the return of a prolonged prothrombin time to normal. Vitamin K will not correct the prothrombin time or the bleeding tendency in jaundiced patients if a major part of the clotting factor defect is due to hepatocellular dysfunction.

Hemorrhagic disease of the newborn is due to deficiency of vitamin K-dependent coagulation factors and is an exaggeration of the physiological deficiency of these factors during the first week of life. The pathogenesis of the syndrome is complex, and vitamin K deficiency is only one aspect. Deficiency may be due to lack of vitamin K-forming bacteria in the neonatal gut, maternal deficiency, or maternal ingestion of antagonist drugs (eg, oral anticoagulants, salicylates). Breast feeding is a risk factor since human milk contains only about 25% of the vitamin K present in cow's milk. In addition, the immature liver synthesizes less of the clotting factors; this is more marked in premature babies. There is also an increased risk of hemorrhagic disease in traumatic and hypoxic deliveries. Phytonadione may be given to the neonate for prevention of treatment, but small doses should be used since a rise in unbound bilirubin may occur, due to the displacement from plasma albumin or reduced hepatic conjugation with glucuronic acid. This effect is more marked with the water-soluble vitamin K analogues, which may also cause hemolysis in patients with glucose 6-phosphate dehydrogenase deficiency and kernicterus in infants. Prophylaxis is more effective when given to the neonate than when given antepartum to the mother; a single intramuscular injection of phytonadione (1.0 mg) is given on delivery to infants at risk because of prematurity, traumatic or hypoxic delivery, or maternal drug ingestion; some centers give prophylaxis to all newborns. In the treatment of hemorrhage, phytonadiene (1.0 mg) is given intramuscularly or intravenously, and repeated every 8 hours if indicated.

Fibrinolytic Inhibitors

These synthetic drugs competitively inhibit activators of plasminogen that convert plasminogen to plasmin. As a result, they prevent breakdown of formed fibrin clot. They are used to prevent or treat bleeding in which local or general fibrinolysis is thought to play a role. Their use carries a risk of formation of unlysable fibrin with consequent thrombotic occlusion. Two fibrinolytic inhibitors are available — aminocaproic acid and tranexamic acid. The latter drug is more potent, acts longer, and has fewer side effects, but it is not available in the United States. Both drugs are well absorbed orally with a peak effect at about two hours; a more rapid effect can be obtained by intravenous injection, but they should be given slowly as hypotension may occur. The dose of aminocaproic acid is 50 to 100 mg/kg body weight every six hours; tranexamic

acid, 10 to 15 mg/kg every eight hours. Elimination is largely by renal excretion. Therefore, accumulation may occur in renal insufficiency and dosage adjustments are required, although their extent is not yet established. Gastrointestinal disturbances and allergic reactions occasionally occur. More serious reactions include local or general arterial or venous thrombosis, which may be due to inhibition of physiological fibrinolysis. Similarly, unlysable clot causing ureteric obstruction and permanent renal failure has been reported in hemophiliacs treated for hematuria.[1]

In hemophilia, whether due to factor VIII deficiency or factor IX deficiency, prophylactic antifibrinolytic agents given before and after dental extraction reduce post-extraction bleeding and factor replacement requirements,[2,3] presumably by inhibition of fibrinolytic enzymes from saliva and buccal tissue. The first dose should be given orally or intravenously before extraction, and oral therapy continued for 7 to 10 days. Synovial fluid contains high levels of fibrinolytic activator that might perpetuate hemarthrosis in hemophilia, but there is insufficient evidence that antifibrinolytic prophylaxis reduces spontaneous musculoskeletal bleeding. Hematuria may respond to fibrinolytic inhibitors (presumably due to inactivation of endogenous urokinase), but in view of the risk of ureteral obstruction, this therapy should only be used as a last resort.

The prostate gland is rich in plasminogen activators which are released into urine during and after prostatectomy, and they may play a role in postoperative hematuria. Prophylactic antifibrinolytic therapy reduces blood loss after prostatic surgery;[4] this type of therapy is started intravenously, during surgery and continued after the operation (intravenously or orally) until macroscopic hematuria is no longer evident.

Endometrial plasminogen activators are increased in women with idiopathic menorrhagia, and fibrinolytic inhibitors reduce menstrual bleeding in this condition[5] as well as in menorrhagia due to intrauterine contraceptive devices; treatment is given from the first day of profuse bleeding. Such therapy is less well established than estrogen/progestogen treatment, and the possibility of thrombotic side effects should be remembered.

Bleeding commonly occurs during thrombolytic therapy with plasminogen activators (urokinase, streptokinase) and is due to depletion of plasma fibrinogen and high levels of FDP. In severe hemorrhage, excessive fibrinolysis can be reversed by cessation of thrombolytic therapy and slow intravenous injection of aminocaproic acid (100 mg/kg every six hours) or tranexamic acid (15 mg/kg every eight hours). In pathological defibrination when laboratory tests suggest that the primary disorder is fibrinolysis rather than DIC, the value of fibrinolytic therapy is not established.

Fibrinolytic inhibitors also inhibit activation of plasma enzymes that consume C1′ inhibitor (C1′ is the first component of the complement system), and they have been used successfully in the long-term prophylaxis and treatment of minor attacks of visceral edema in patients with the rare disorder of hereditary angioedema due to C1′ inhibitor deficiency.[6]

Blood Products

The cost of collection, processing, storage and delivery of blood and blood products makes them expensive. Since the products are heterogeneous mixtures of proteins from other individuals, the risk of immunologic reactions and of the transmission of diseases, particularly viral hepatitis, always exists; these risks are dose-related. The proper blood product must be selected for the appropriate degree of correction of the individual patient's hemostatic defect or defects. Specific therapy is most economical. Because of the risk of circulatory overload, the less concentrated products, such as plasma, can only be administered in limited quantities. Thus, blood and blood products should be used cautiously, and the relative risks of bleeding and adverse effects should be carefully balanced. The type and degree of hemostatic defect should be determined by laboratory tests, and close collaboration with a specialist in blood disorders is desirable.

Adverse Effects. (1) *Circulatory overload.* Pulmonary edema may occur following infusion of large quantities of blood or plasma, particularly in the normovolemic, the severely anemic, the elderly, and patients with heart disease. The infusion should be stopped and appropriate treatment of pulmonary edema instituted. Preventive measures include slow infusion and the administration of a diuretic.

(2) *Allergic reactions.* Allergic reactions to gamma globulins, leukocyte antigens, or platelet antigens are more common in patients with an allergic history and in those who have received multiple infusions of blood products. The incidence of reactions may be reduced, but not entirely eliminated, by prophylactic administration of an antihistamine or corticosteroid: this should be considered in such patients, particularly those with a history of previous reactions. These drugs should be given separately to the patient and not added to the blood product. Minor reactions (headache, malaise, nausea, urticaria, pyrexia, skin edema) may be treated by stopping or slowing the infusion and the administration of an antihistamine, such as chlorpheniramine (10 mg by slow intravenous injection, then 4 mg orally every 4 to 6 hours). Major reactions (asthma, laryngeal edema, anaphylaxis) should be treated immediately by stopping the infusion and giving subcutaneous or intramuscular epinephrine, 0.1 to 0.5 mg (0.1 to 0.5 ml of a 1:1000 solution), intravenous chlorpheniramine, 10 to 20 mg, and intravenous hydrocortisone, 100 to 200 mg. Epinephrine is by far the most effective antidote. Oxygen and cardiopulmonary support may also be neces-

sary.

(3) *Hemolytic reactions.* These are usually complications of whole blood transfusions, but plasma and plasma fractions also contain small amounts of iso-antibodies, and repeated large infusions may cause hemolysis.

(4) *Pyrogenic reactions.* Fever may be part of an allergic or hemolytic reaction, or due to pyrogens from bacterial contamination of the blood product or transfusion apparatus. Septic shock and death may result. Careful aseptic technique and disposable apparatus have reduced such complications.

(5) *Viral hepatitis.* As with infective hepatitis, overtly jaundiced patients represent only a fraction of those with post-transfusion hepatitis, since most cases are subclinical and revealed only by screening for abnormal liver function.[7] Blood products prepared from large pools of donors, such as clotting factor concentrates, are particularly hazardous since the virus from a single donor can be distributed throughout the batch and remain infective. Patients who have not received such concentrates frequently in the past are at greatest risk.[8] Persons with a history of jaundice or drug addiction should be excluded from blood donation; the hepatitis risk is also greater in products derived from the blood of paid donors as compared to volunteer donor blood,[7] and volunteer blood is preferable. About 25% of blood donors who are carriers of viral hepatitis can be identified by screening for the surface antigen of hepatitis B (classical long-incubation serum hepatitis). The risk of transmitted hepatitis can be further reduced by screening potential donors and blood products. More recently serologic tests have been developed for hepatitis A (classical short-incubation infectious hepatitis), which can also be transmitted parenterally. However, most cases of post-transfusion hepatitis are not due to well-characterized viruses.[9]

Principles of Replacement Therapy in Clotting Factor Deficiencies

In patients with hemorrhage due to thrombocytopenia, the level of platelets may be raised by the infusion of fresh blood, platelet-rich plasma, or platelet concentrate. In those with coagulation factor deficiencies, the deficient factor or factors as well as the extent of deficiency should both be identified if possible. General guidelines for adequate replacement therapy have been defined by observation of clinical response in large numbers of patients treated in special units and are best established for the hemophilias. However, they are only guidelines, since within- and between-patient variations in hemostatic response to replacement therapy are considerable.

Blood products used in replacement therapy are as follows:

(1) *Whole blood* and *plasma* which contain stable coagulation factors but not the labile factors V and VIII; *fresh plasma* and *fresh frozen plasma* (F-F-P) contain these factors.

(2) *Cryoprecipitate* and *factor VIII concentrates* (antihemophilic factor) (Factorate, Hemofil, Humafac) which are rich in factor VIII and are used in the management of hemophilia A and von Willebrand's disease.

(3) *Factor IX concentrates* (prothrombin complex concentrates) (Konyne, Proplex) which are rich in factors II, VII, IX, and X and are used in the management of hemophilia B (factor IX deficiency) as well as acquired defects of these factors.

(4) *Fibrinogen concentrates* (Parenogen) which are used in defibrination syndromes.

Hemophilia A

This is the most common congenital bleeding disorder. Patients with hemophilia A are deficient in factor VIII (antihemophilic factor) activity. The severity of bleeding depends on plasma factor VIII activity.[10] When less than 5% of normal, bleeding into muscles and joints commonly occurs, either spontaneously or following minor trauma; spontaneous bleeding is particularly common in patients with a level of 1% or less. Spontaneous bleeding is uncommon in patients with levels of 5 to 25%, but can occur after minor trauma; serious bleeding may occur after major trauma or surgery. Patients with levels of 25 to 50% of normal (borderline levels for normal hemostasis) bleed excessively only after major trauma or surgery.

The plasma level of factor VIII required to treat bleeding, or to prevent bleeding after surgery, depends on the type, size, and duration of the trauma or hemorrhage.[10] Traumatic bleeds, large bleeds, and bleeds in muscles, bleeds that endanger the airway or compress arteries or nerves and bleeds not treated within a few hours of onset require higher plasma levels. For early spontaneous hemarthroses a level of 5 to 20% immediately after infusion is sufficient. Large musculoskeletal bleeds, especially in dangerous sites, and dental extractions will require a post-infusion level of 20 to 40%. In major surgery, trauma, or hemorrhage in the central nervous system, immediate levels of 80 to 100% are desirable.

Since the half-life of infused factor VIII in the circulation is about 12 hours, the level after 24 hours will be only one-quarter of the initial level. Doses of factor VIII should be given before the plasma level falls dangerously low, and in major bleeds, trauma, or surgery infusions may have to be repeated every 8 to 12 hours. For optimal replacement therapy, the factor VIII level before and after infusion should be monitored in such patients.

The duration of treatment also depends on the type of bleeding. A single dose may be sufficient for a small hemarthrosis treated early; larger bleeds may require several daily doses and major surgery may require 10 to 14 days of treatment. The frequency of doses may be reduced from every 8 hours to every 24 hours if progress is satisfactory. Or-

thopedic surgery or wound complications may necessitate even more prolonged treatment. At some centers selected patients are given regular prophylactic factor VIII infusions.

The amount of material necessary to achieve a given plasma factor VIII level depends on the type, potency, and volume of the material as well as the patient's plasma volume. Approaches to dosage calculations are available elsewhere.[10]

Factor VIII levels in whole blood and plasma decline rapidly with storage and hence these are inadequate materials for factor VIII replacement. In the treatment of hemophilia, they should be used solely for red cell and plasma volume replacement. Fresh plasma or fresh frozen plasma may be used to treat minor bleeds, since a rise in factor VIII level of 20% may be achieved in a 70 kg man by infusion of about 1 liter. Problems of volume overload and time delays in preparation and infusion of plasma are reduced by the use of plasma fractions rich in factor VIII — cryoprecipitate or factor VIII concentrates.

Cryoprecipitate

Cryoprecipitate is made by rapid freezing and cold-thawing of plasma, and is easily prepared in hospital blood banks. It contains 40 to 80% of the original factor VIII activity and is rich in fibrinogen.[11] An average bag of cryoprecipitate from a pint of blood contains about 60 units of factor VIII (1 unit of factor VIII activity is the amount present in 1 ml of fresh pooled citrated normal plasma) and an average dose for an early musculoskeletal bleed is 600 to 900 units (10 to 15 bags). A small dose may be drawn up and infused in large syringes; larger doses are pooled and infused via a blood product drip set. Gel formation suggests activated clotting factors and the pack should not be given. Large doses of cryoprecipitate may be given to achieve high plasma factor VIII levels (up to 100%) without hypervolemia for the treatment of serious bleeding and for hemostatic cover of major surgery; this has revolutionized the management of hemophilia in the last ten years. Cryoprecipitate has been used for home treatment but is less satisfactory than factor VIII concentrate since it must be stored frozen and then thawed. The main disadvantage of cryoprecipitate is the variation in potency of different batches. A high plasma fibrinogen level results from frequent infusions and occasionally causes hemolysis, platelet dysfunction, and transient proteinuria.

Antihemophilic Factor (Factor VIII Concentrates) (Factorate, Hemofil, Humafac)

In recent years lyophilized concentrates of factor VIII have been produced from human plasma or cryoprecipitate. These concentrates are stable for several months when stored at about 4°C and may be kept in a domestic refrigerator, allowing early treatment of minor bleeds in the home of selected patients. Treatment may be given by the patient himself, a relative, nurse, or general practitioner. Home treatment has undoubtedly improved the quality of life of patients with severe hemophilia; however, careful selection, education and follow-up of patients is required.

Each batch of concentrate is assayed for factor VIII activity and the amount per vial (usually 150 to 500 units) is stated on the label. The product is reconstituted with about 20 ml of Water for Injection with sterile precautions; this takes about 10 minutes. Gel formation suggests activated clotting factors and the vial should not be given. The concentrate is drawn up in a large syringe and infused at a rate not exceeding 10 ml per minute, otherwise vasomotor reactions may occur.

Unlike cryoprecipitate, the potency of factor VIII concentrates is known and the plasma level of factor VIII is more predictable. One problem with the concentrates is that the large pool of donors increases the risk of hepatitis; the risk is greatest in patients with mild hemophilia who have not received multiple infusions of blood products in the past, and some physicians prefer to treat minor bleeds in such patients with single-donor or small products.[8]

Patients With Factor VIII Inhibitors

At some stage in their lives, about 10% of treated hemophiliacs develop antibodies to factor VIII that destroy its activity. The appearance of an inhibitor does not correlate with the amount, frequency, or type of factor VIII replacement therapy, and should be suspected if the clinical response or plasma factor VIII level response to replacement therapy is poor. An inhibitor assay should be done routinely prior to surgery or dental extraction. If further infusions of factor VIII are given, their activity is rapidly destroyed by the inhibitor, and, in addition, the inhibitor level often rises. Left untreated, the antibody level slowly falls over a year or two, sometimes to undetectable levels, but returns within 5 to 10 days of further factor VIII infusion. Therefore, in patients with high levels of inhibitors, only serious bleeds should be treated. Once the decision to treat has been made, treatment should be intensive with large doses of factor VIII before the antibody levels rise.[12] Removal of the antibodies by plasmapheresis, and suppression of the antibodies by corticosteroids or azathioprine have been tried, but the results are usually disappointing. Bypassing of the factor VIII state of the coagulation cascade by prothrombin complex concentrates (see below) is more promising;[13,14] however, there is a risk of thrombosis with these products and their use is still experimental.

Occasionally factor VIII inhibitors develop in non-hemophiliacs, especially the elderly, those with immune disorders, and postpartum women. The manifestations are similar to hemophilia, and treatment is the same.

Von Willebrand's Disease

The characteristics of this congenital bleeding

disorder are: (1) a moderate deficiency of factor VIII activity; (2) a prolonged and progressive rise in factor VIII following infusion of plasma or serum, which presumably contains an inducer of endogenous factor VIII synthesis; (3) a prolonged skin puncture bleeding time, presumably due to various morphological and functional abnormalities of platelets, the most sensitive of which is ristocetin-induced aggregation. The interrelationship of these characteristics is unclear and the extent of defect varies between patients, suggesting that the syndrome may actually be a group of disorders. Bleeding severe enough to warrant treatment can usually be controlled by raising the plasma factor VIII to an appropriate level, as in the treatment of hemophilia A. Small daily doses of fresh frozen plasma are often sufficient since they induce endogenous factor VIII formation, although 24 to 48 hours may elapse before peak levels are reached. More rapid correction of factor VIII levels may be achieved with cryoprecipitate or factor VIII concentrates, although they may be less effective stimulants of factor VIII synthesis. These plasma fractions may also correct the prolonged bleeding time and platelet functional abnormalities.

Hemophilia B (Christmas Disease)

Hemophilia A and B are clinically indistinguishable, but B hemophiliacs have congenital deficiency of factor IX activity rather than factor VIII. The levels of factor IX required for hemostasis are similar to those of factor VIII required in hemophilia A, and the principles of replacement therapy are also similar even though the products used are different.

The half-life of infused factor IX in the circulation is longer than that of factor VIII — about 24 hours — hence once daily doses are sufficient for most bleeds. Doses given every 12 hours may be required to maintain high plasma levels in major bleeds or surgery. The recovery of factor IX activity in the circulation is less complete than the recovery of infused factor VIII, possibly because the smaller molecular weight of factor IX allows extravascular distribution.[10]

Stored whole blood and plasma lose factor IX activity much more slowly than factor VIII activity, but the risk of volume overload limits their use for any but minor bleeds. Fresh plasma or fresh frozen plasma may be used to treat minor bleeds; a rise in factor IX level of 5 to 10% may be achieved in a 70 kg man by infusion of 1 to 1.5 liters of fresh plasma.

Factor IX Concentrates (Prothrombin Complex Concentrates) (Konyne, Proplex)

These preparations are used to treat major bleeds or to cover major surgery in patients with hemophilia B. Plasma levels of 50 to 100% can be achieved by infusion of relatively small volumes. Factor IX concentrates are much more convenient for treating minor bleeds than fresh frozen plasma; however, as in hemophilia A some physicians prefer

Tablets
Percocet®-5 (II)

DESCRIPTION Each tablet of PERCOCET®-5 contains 5mg oxycodone hydrochloride (WARNING: May be habit forming), 325mg acetaminophen (APAP).

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone or acetaminophen.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCOCET®-5, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCOCET®-5 is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCOCET®-5 should be cautioned accordingly.

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCOCET®-5 may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCOCET®-5 should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCOCET®-5 should not be administered to children.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions The administration of PERCOCET®-5 or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients PERCOCET®-5 should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. PERCOCET®-5 is given orally. The usual adult dose is one tablet every 6 hours as needed for pain.

DRUG INTERACTIONS The CNS depressant effects of PERCOCET®-5 may be additive with that of other CNS depressants. See WARNINGS.

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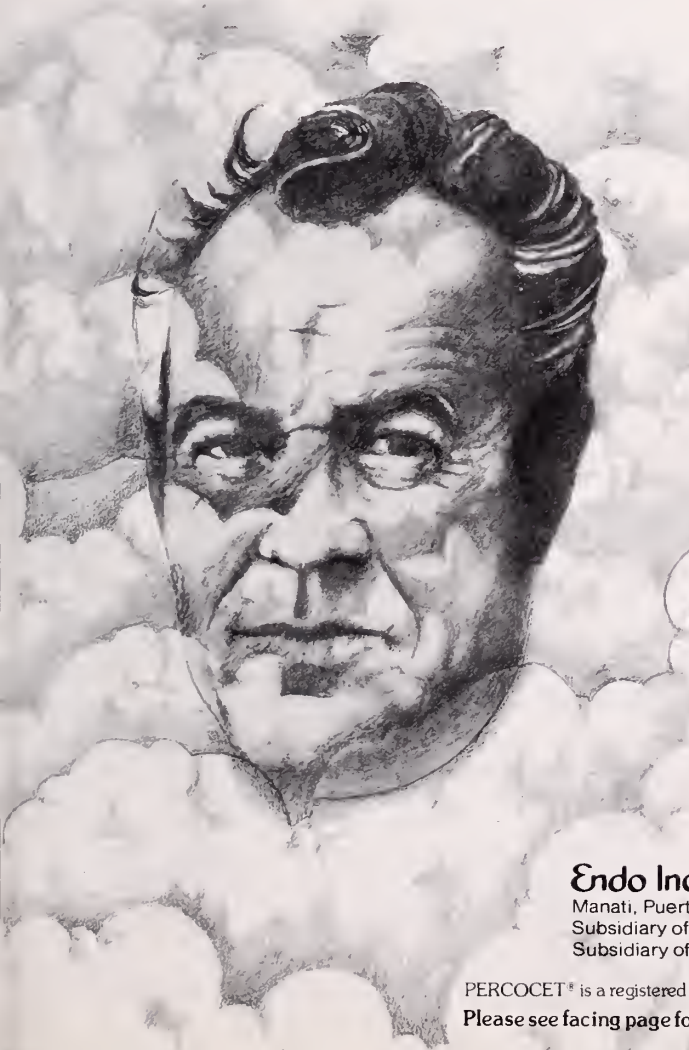

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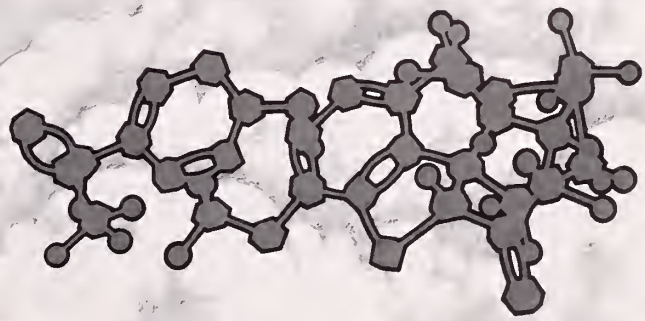

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Please see facing page for Brief Summary of prescribing information.

to treat minor bleeds with single-donor or small pool plasma since the risk of hepatitis is less.

At present, factor IX cannot be separated from factor II (prothrombin), factor X, and (not in all preparations) factor VII. Factor IX concentrates are therefore also termed prothrombin complex concentrates, and they may be used for treating bleeding in the rare congenital deficiencies of factor II, factor X, or factor VII, as well as the much more common acquired deficiencies of these factors — liver disease (see below) and oral anticoagulant therapy.

As with factor VIII concentrates, factor IX concentrates are lyophilized, stored in a refrigerator, and reconstituted with sterile water. They are suitable for home therapy. Gel formation suggests activated clotting factors (see below), and the vial should not be given. The rate of infusion should not exceed 10 ml per minute. The amount of assayed factor IX, and sometimes the level of other factors, is stated on the vial.

Factor IX concentrates are prepared from large pools of donors and have a fairly high risk of hepatitis. Thromboembolic complications, which include local thrombosis and disseminated intravascular coagulation, can be fatal.[15,16] Such complications may arise from activation of clotting factors during the manufacturing process; screen tests for thrombogenicity are now performed and some preparations contain heparin to neutralize activated factors. Some "activated" preparations have been used in the treatment of patients with factor VIII inhibitors (see above); however, relatively "non-activated" concentrates have also been used successfully.[14]

Other Congenital Coagulation Disorders

Fibrinogen (factor I) may be given to patients with afibrinogenemia or abnormal fibrinogens (dysfibrinogenemia) as plasma, cryoprecipitate or fibrinogen concentrate (see section on defibrination below). Deficiency of factors II, VII or X can be treated with plasma or prothrombin complex concentrates as mentioned above. Deficiency of factors V or XI can be treated with fresh or fresh-frozen plasma. Factor XIII, which has been omitted from Figure I for clarity, converts soluble fibrin monomer to insoluble fibrin polymer; congenital deficiency may be treated with fresh frozen plasma.

Acquired Deficiency of Factors II, VII, IX and X

Acquired deficiency of "prothrombin complex" factors may be due to vitamin K deficiency, oral anticoagulant therapy, or hepatocellular dysfunction. In bleeding due to vitamin K deficiency or oral anticoagulant therapy, vitamin K may control the hemorrhage (see section on vitamin K above) but in severe bleeding replacement of coagulation factors may be indicated, using plasma or prothrombin complex concentrates (see above).

Bleeding in patients with hepatocellular disease does not usually respond to vitamin K, and factor replacement may be required in serious bleeding or prior to surgery. However, recovery of infused factors in the circulation, and clinical response, are often disappointing. Fresh plasma or fresh frozen plasma may be used, but dosage is limited by volume overload. Prothrombin complex concentrates are more potent but carry the risk of viral hepatitis and thromboembolic complications;[17] the latter may occur because the liver normally either removes activating clotting factors from the circulation or inactivates them. The relative contribution of the deficient factors to bleeding is uncertain. Similarly, the relative value of plasma, concentrates containing factor VII, and concentrates lacking factor VII is unclear. It is logical to monitor individual factor levels in addition to coagulation times and to aim for "hemostatic" levels — factor II, 40% of normal; factor VII, 10%; factor IX, 40% and factor X, 20%. However, the efficacy, safety, and choice of blood products in liver disease requires further study. Patients with liver disease may also have low levels of platelets (consider replacement if the platelet count is under 50,000 per ml), fibrinogen (replace with plasma or fibrinogen concentrate to 100 mg/100 ml), and factor V (replace with fresh or fresh frozen plasma to 15% of normal) — all of which may contribute to bleeding.

Defibrination Syndrome

In bleeding due to defibrination, treatment of the underlying cause and effective supportive care are essential. In the special case of bleeding during thrombolytic therapy with urokinase or streptokinase, the use of fibrinolytic inhibitors may be considered (see above). Plasma fibrinogen may be raised to a hemostatic level (100 mg/100 ml) with blood, plasma, cryoprecipitate, or fibrinogen concentrate.

Fibrinogen Concentrate (Parenogen)

Fibrinogen is available as a freeze-dried powder which is stored under refrigeration and reconstituted with sterile water. The risk of hepatitis is high (up to 20%), and many physicians prefer to use cryoprecipitate if a more potent source of fibrinogen than plasma or blood is required.

In disseminated intravascular coagulation, other clotting factors are consumed, particularly the labile factor VIII and factor V. Platelets may also be consumed. Factor VIII may be replaced by fresh plasma, cryoprecipitate, or factor VIII concentrates; factor V by fresh or fresh frozen plasma; and platelets by platelet concentrates. Fresh whole blood provides volume, red cells, platelets, and all clotting factors and may be valuable in urgent situations. However, bleeding may be due largely to circulating anticoagulant fibrinogen/fibrin degradation products (FDP) rather than to deficiency of clotting factors or platelets.

The use of heparin and fibrinolytic inhibitors in defibrination syndromes is controversial. Management of defibrination syndrome is discussed in detail elsewhere.[18]

Massive Transfusion of Stored Blood

When bleeding patients receive massive transfusions of stored blood (eg, more than 8 units in 24 hours), plasma levels of platelets and the labile coagulation factors (VIII and V) will fall and thereby contribute to bleeding. Two units of fresh blood or fresh frozen plasma per 10 units of blood are usually sufficient to prevent or treat these deficiencies; additional platelet transfusions may be required if thrombocytopenia is severe. The large quantities of infused citrate lower plasma calcium levels, and this may also contribute to bleeding. To prevent calcium depletion, slow intravenous injection of 10 ml of 10 percent calcium gluconate per 5 units of transfused blood has been recommended.

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COST CONTAINMENT INITIATIVES

The Blue Cross and Blue Shield of Maine Board of Directors has been discussing cost containment as part of its regular meetings, and a list of approaches was developed for consideration.

The discussion came out of a number of issues, including increasing Blue Cross and Blue Shield rates, the feeling on the part of some Providers that Blue Cross and Blue Shield of Maine is trying to "run" the health system, the fact that while physicians collect only ten to twenty percent of the health care dollar, they control another forty-five to seventy percent, and the point that ongoing analysis of the costs generated by all areas of the health field, including Blue Cross and Blue Shield of Maine, is in order.

The approaches discussed by the Board and reported by Richard Stride, Chairman of the Board, in a recent speech to a group of physicians, include:

1. We (Blue Cross and Blue Shield of Maine) should continue to scrutinize our own expenses, searching for new management techniques which would result in greater cost efficiency.

2. We should make available, in as nonthreatening a mode as possible, the information we accumulate on cost containment activities like home health care, peer review, data analysis, duplication of services and cost comparisons.

3. We should develop systems of reward for participants who do make progress in keeping down costs. We should solicit suggestions on cost containment from everyone: subscribers, contracting participants, the general public.

4. We should recognize the fact that there is an awful lot that boards of directors of hospitals, as well as of Blue Cross and Blue Shield do not know, and we should do much much more toward opening lines of communication between these governing bodies of the health-care institutions and our own board. And we cannot afford, any of us, to lose sight of the fact that ours is a symbiotic relationship. In that spirit, we are not trying to run other people's businesses; we are offering to exchange information that may well help us all. We should preserve the longstanding relationships of professionals and providers and consumers with the Blue Cross and Blue Shield Board of Directors.

5. We should continue to expand our various educational programs, emphasizing the startling fact that medical treatment affects only about ten percent of the indices commonly used to measure health. The remaining ninety percent are beyond the control of physicians and relate to our own self discipline concerning diet, exercise, life style and environment.

6. Finally, we should be very careful that we do not rely too heavily on the other fellow to do the job.

Necrologies

Edward C. Porter, M.D.

1921-1977

Dr. Edward C. Porter, 56, of Bangor, Maine, a veteran Radiologist at the Eastern Maine Medical Center and former Mayor of Bangor, collapsed and died while duck hunting at Milbridge on October 18, 1977.

Born in Malden, Massachusetts on April 18, 1921, he was the son of Ward F. and Alberta F. Porter.

He was graduated from Dartmouth College and received his medical degree from Harvard Medical School in 1945. Dr. Porter interned at the Rochester General Hospital in New York and served residencies at the Mary Hitchcock Hospital in Hanover, New Hampshire and Mt. Auburn Hospital in Cambridge, Massachusetts.

Dr. Porter practiced in Hartford and Newington, Connecticut and in 1955 joined the attending staff in radiology at the Eastern Maine Medical Center. He had served as chief of the Medical Center's nuclear medicine section, and in 1972 was appointed chief of the radiology department.

He was a member of the Penobscot County Medical Society, the Maine Medical Association and the American Medical Association. He was also a fellow of the American College of Radiology, a member of the Radiology Society of North America, the Society of Nuclear Medicine and the American Board of Radiology and Nuclear Medicine.

Active in various community affairs, Dr. Porter was twice elected to the Bangor City Council, serving as Mayor in 1969. He also served on the Bangor School Committee, the Bangor High School Committee, and assisted in the Dow AFB redevelopment planning. In 1971, he was president of the steering committee for a new building at Eastern Maine Medical Center. It was this drive, the first in half a century, which eventually led to the construction of the new wing.

Surviving are his widow, Claire, and seven children.

Thomas A. Devan, M.D.

1884-1977

Dr. Thomas A. Devan, 93, of St. Petersburg, Florida, died suddenly on November 26, 1977.

He was born in Brooklyn, New York on January 31, 1884, the son of Thomas A. and Mary A. Devan.

Dr. Devan was graduated from Rutgers University and received his medical degree from Johns Hopkins University School of Medicine in 1910. He interned and served a residency at Columbia-Presbyterian Medical College.

He was House Physician at the Peter Bent Brigham Hospital, served as Professor of Hygiene at Rutgers, Assistant Director of Strong Memorial Hospital and Director of the Massachusetts General Hospital and the Eastern Maine Medical Center.

An honorary member of the Penobscot County Medical Society and the Maine Medical Association, he received a 50-year pin in 1960, a 55-year pin in 1965, a 60-year pin in 1970 and a 65-year pin in 1975.

Surviving is his widow, Emeline M. Devan.

Robert M. True, M.D.

1924-1978

Dr. Robert M. True, 53, of Freeport, Maine, died unexpectedly in Riverdale, Maryland on January 9 while attending a medical seminar.

Born in Rutland, Vermont on August 13, 1924, he was the son of George L. and Phyllis M. True.

He was graduated from Bowdoin College and received his medical degree from the University of Vermont College of Medicine in 1952. Dr. True interned and served a residency at the Waltham Hospital in Massachusetts.

Dr. True practiced family medicine in Weston, Massachusetts for 20 years and located in Freeport in 1974.

He was a member of the Cumberland County Medical Society, the Maine Medical Association and the American Medical Association. Dr. True was chief of staff of the Waltham Hospital medical staff; chief of the Department of Family Practice, director of the Family Practice Residency Program, director of the Model Family Practice Unit of the Maine Medical Center, and director of the Casco Bay Health Center.

Surviving are his parents; his widow, Marilyn B. True of Freeport; and two daughters, the Misses Caron M. of Medford, Massachusetts and Nancy B. of Cambridge, Massachusetts.

Paul A. Millington, M.D.

1911-1978

Dr. Paul A. Millington, 66, of Camden, Maine, died at a Camden hospital on January 17.

He was born in Fall River, Massachusetts on October 17, 1911, the son of William and Louise Millington.

A graduate of Tufts University, he received his medical degree from Tufts University School of Medicine in 1937 and interned at the Burbank Hospital in Fitchburg, Massachusetts.

Dr. Millington located in Newport in 1939 where he was affiliated with the Pownal State School. He had practiced in Camden as Family Practitioner, Obstetrician and Anesthesiologist for the past 35 years, and was a member of the active staff of the Camden Community Hospital and Health Care Center.

He was a member of the Knox County Medical Society, the Maine Medical Association and the American Medical Association.

Surviving are his widow, Florence of Camden; a son, Donald E. of Camden; two brothers, Roy of Lunenburg, Massachusetts and Burton of Evanston, Illinois; and two grandchildren.

County Society Notes

York

The October meeting of the York County Medical Society was held on October 12, 1977 at the York Hospital, York Village, Maine.

The program was as follows: Social Hour, 6:30-7:30 p.m.; Dinner, speaker and business meeting followed.

After a delicious dinner, the featured speaker was Dr. Douglas R. Hill of South Portland, President of the Maine Medical Association. The subject concerned matters of importance to the Maine Medical Association. This included a discussion of medical malpractice, medicaid fees, "Certificate of Need," and the hiring of the Assistant Executive Director of the Maine Medical Association, etc.

This talk was presented in a very intriguing and interesting manner. He was introduced by President Lawrence R. Hazzard, who thanked him for the presentation, following it.

Dr. Carl E. Richards congratulated Dr. Hill on this talk, stating that it was one of the best and most interesting he had ever heard.

Immediately following this talk, Dr. Hazzard called the meeting to order. In the interest of time, the minutes of last meeting were dispensed with. There was no old business.

Among the new business was the presentation of new applications for membership in the York County Medical Society. These included Drs. Paul Lorenzon, Joseph Inzerillo, Thomas Collins, Robert Sholl, Jonathan Shill and Arthur Spearing. All were duly elected to membership. Another item discussed in this category was the Diabetes Program in York County.

Announcements included the annual meeting of the York County Medical Society which would be held on Wednesday, January 11, 1978 with the time and place to be announced.

Another item mentioned was the interim meeting of the House of Delegates of the Maine Medical Association to be held at Mid-Maine Medical Center, Waterville, Maine, in December.

The report of the House of Delegates of the Maine Medical Association held on Saturday and Sunday, June 11 and 12, 1977 at the Treadway-Samoset, Rockport was given by Dr. Richards. At this time, he discussed the budget of the Maine Medical Association for 1978. He also mentioned the committee on nominations. He brought up the question of an appointment of an assistant executive director for the Maine Medical Association.

A report of the Committee on Recruitment, Aid and Placement was also given and reports of other committees were presented by him in brief.

Resolutions from various county societies and the Executive Committees were also taken up by him. There were twenty physicians and three guests present.

The meeting was adjourned at 9:20 p.m.

MELVIN BACON, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association meeting was held at the Holiday Inn in Augusta on December 15, 1977. The wives were in attendance and attendance was not counted.

The only business discussed at this meeting was the election of Dr. H. Winston Kipp to membership.

Mr. Jolyon Sprowle of Bates College presented a computerized discussion of the energy utilization situation in the world today.

The Kennebec County Medical Association met at John Martin's Manor in Waterville on January 19, 1978, with sixty-two members and two guests in attendance, to hear a most enlightening and interesting discussion of the possible physician-owned malpractice insurance company, by Dr. Patrick A. Dowling and Mr. John Schroeder. The members of the Association heard this presentation with great interest.

Communications from Dr. Thomas F. Shields regarding a Seminar on Negotiations were read, as well as a letter from Senator Olympia Snowe concerning the certificate of need legislation.

The applications of Drs. Lawrence B. Mutty and Danielle V. Mutty were voted on and they were accepted into membership.

O. THOMAS FEAGIN, M.D., *Secretary*

Penobscot

The December meeting of the Penobscot County Medical Society was held on December 20, 1977, at Pilot's Grill in Bangor.

The meeting was opened by the President, Dr. Philip G. Hunter and the minutes of the November meeting were approved. President Hunter then summarized some of the more significant proceedings at the recent House of Delegates meeting held in Waterville on December 10th. It was noted that negotiations are underway between the M.M.A. and the Department of Human Services regarding the recent suit of the M.M.A. against the Department of Human Services concerning the 10% reduction in physician payments and the new fee schedule. It seems the Department of Human Services is anxious to have the suit withdrawn. It was also noted that the search committee for the relocation of the M.M.A. office from Brunswick to Augusta has found little available land and, what is available, to be quite expensive. Consideration is being given to activate the $100 assessment per member for the building program of the M.M.A. that was passed at the 1976 annual meeting. It was reported by Dr. Dowling of the Ad-Hoc Committee on malpractice that the firm of Johnson and Higgins in Boston has, indeed, recommended to go ahead with plans for a doctor captive insurance company for the State of Maine. More details on this will be forthcoming and will be available for discussion at the county society level.

Two applications for membership were presented: Drs. Harry S. Tamm and Robert M. Hoffmann of Bangor; both were unanimously accepted.

There was considerable discussion regarding the $100 assessment for a building program. It was felt that such cost ought to be borne by the membership over an extended period of time and not by a single group of doctors on a lump-sum basis in a given year. A motion was made, seconded and passed that President Hunter is to appoint a committee to draw up a resolution for presentation to the annual meeting of the M.M.A. in June 1978, that would rescind the $100 assessment.

There followed an informative discussion by Mr. Chester Dosdall, the manager of the Maine J.U.A., concerning the mechanism of operation of the J.U.A., its premium schedules and outlook for the future in regards to the malpractice insurance situation. As the Society had learned about prospects for the doctor captive insurance company at last month's meeting from a representative of the Johnson and Higgins firm, it was interesting to hear a discussion of the problem from the insurance companies' point of view.

The meeting was adjourned at 10:15 p.m.

H. CLEMENT JURGELEIT, M.D., *Secretary*

Aroostook

A regular meeting of the Aroostook County Medical Society was held in the ballroom of the Northeastland Hotel, Presque Isle, Maine on January 18, 1978, at 8:15 p.m., with fourteen members present.

I. The president, Dr. Arthur D. Pendleton, called the meeting to order at 8:15 p.m.

II. *Previous Minutes.* The minutes of the previous meeting were deferred due to the absence of the secretary.

III. *Communications.* The reading of communications was deferred to new business.

IV. *Reports.*

1. Dr. Eric F. Nicholas presented the report of the December meeting of the Executive Committee of the Maine Medical Association. In addition, Dr. Nicholas reported on matters before several committees including the following:

a. School Health. The Committee has been requested to review the school nurse program with the recommendation that all

physical examinations should be complete and thorough.

b. Health Care Financing. The Committee updated the Blue Cross-Blue Shield program to take effect May 1, 1978.

c. Building Committee. The Building Committee is looking for new quarters in Augusta.

d. Malpractice Committee. The Committee resolved to endorse the formation of its own insurance company to underwrite the malpractice insurance for physicians in Maine.

e. Health Legislation. The matter of a Certificate of Need Bill requiring HSA review for expenditure of $150,000 for equipment for hospitals and physicians' offices was presented. A discussion followed concerning Certificate of Need legislation. Dr. Chow, seconded by Dr. Helfrich, moved that "The Aroostook County Medical Society is opposed to any Certificate of Need legislation that applies to physicians' offices." The motion was carried; 12 in favor, 2 opposed. The membership further recommended that a letter be drafted from the Society to Senator Roland Martin indicating the Society's support and satisfaction regarding his vote on Certificate of Need legislation.

V. *Old Business.*

Revision of Bylaws. It was recommended by the membership present that the Bylaws of the Society be revised and updated. Dr. Helfrich was appointed to Chair a committee of three which would study the existing Bylaws and prepare a preliminary report as to revision for the Society, such reports being due at the meeting in March.

VI. *New Business.*

1. Membership applications. The membership applications of Dr. Carol St. Pierre of Washburn and Dr. Laurence Watterson of Presque Isle were approved by the membership, pending final review by the Credentials Committee. The membership requested that the Maine Medical Association review the status of Dr. Frederick Allen of Fort Kent and advise the Society as to any action required. An application form is to be sent to Dr. Usagonker of Fort Fairfield.

2. HSA proposed plan for State of Maine. Dr. Chow presented a comprehensive review of the proposed HSA plan for the State of Maine and pointed out that the two formulas which were applied to the central Aroostook County area were applied incorrectly, resulting in incorrect determinations as to bed allocations. Dr. Chow further indicated that there were two basic objections to the proposed plan by providers locally. The first objection had to do with the fact that there was insufficient time to review the proposed plan and comment appropriately. The second objection had to do with the fact that Aroostook County as a remote, sparsely populated area, is quite different from the larger metropolitan areas in the southern part of the State. Wherever, in consideration, the HSA has proposed a sub-area council for Aroostook County with 21 members, 5 of the members being from the primary HSA Board and the other 16 members from Aroostook County.

3. Legislative contacts. The list of legislative physician contacts was reviewed. Dr. Paul Nicholas' legislative contacts are to be referred to Dr. Johnson of Fort Kent.

4. RAISE Regional Medical Library Grant. A request is received from RAISE regarding the endorsement of a fulltime medical librarian to serve the county's hospitals on a circuit riding basis. This grant would be coming from the National Library of Medicine. The matter was referred to Dr. David Skinner for further followup and discussion with local medical librarians. Dr. Skinner is to report back to Dr. Pendleton by the end of the month.

5. CAT Scanners. Dr. O'Brien reported on a meeting of physicians in Augusta regarding Statewide planning for procurement and utilization of CAT scanners.

6. Nominees for Executive Committee and Delegates. The membership requested that a letter be sent to the Presidents of each Medical Staff in the county requesting nominations for one member to serve on the Executive Committee, two members to serve as delegates, and two members to serve as alternate delegates.

7. Education Committee. Dr. Pendleton appointed Dr. David H. Skinner to serve as a member of the Education Committee of the Society.

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8. Minutes of meeting. Dr. Nicholas moved that copies of all minutes of the Society's meetings should be sent to the President of the Society, the representative on the Executive Committee, and a copy to the Maine Medical Association. Motion was carried unanimously.

There being no further business, the meeting was adjourned at 9:45 p.m.

LAURENCE J. MCCARTHY, M.D., *Secretary Pro-tem*

Washington

A regular meeting of the Washington County Medical Society was held on January 17, 1978 at the Peavy Memorial Library, Eastport, Maine, with seven members present.

I. Minutes of last meeting read and approved.

a. From the minutes, members were asked, by written ballot, if they would be willing to set up a committee for Washington County Medical Society to meet with Washington County Health Plan, or similar organizations, to discuss matters of mutual concern and report back to the Medical Society.

b. These ballots were sent out and the majority were in favor of appointing a committee to act as a liaison between the Medical Society and the Washington County Health Plan, or similar organizations.

c. Dr. James C. Bates, President of the WCMS, appointed Drs. Carl K. Aselton, Jr. of Milbridge, G. Bernard Shaw of Machias and Hazen Mitchell of Calais to be members of this Committee.

II. Dr. Robert G. MacBride, Delegate from the Washington County Medical Society to Maine Medical Association reported on the Fall meeting of the House of Delegates held on December 10, 1977 in Waterville, Maine.

a. The Maine Medical Association is in the process of trying to set up its own Malpractice Insurance Company.

b. He also reported that the Association was seeking ways and means of having the Association moved from its present quarters in Brunswick, at Bowdoin College, to a site near the capital in Augusta. Considerable discussion apparently has taken place as to whether the Association should rent or build.

c. Dr. MacBride also stated that in order to finance this, it might be necessary to access each member $100, which has already been voted on.

III. Dr. Randolph S. Silver, Medical Advisor of Maternal Infant Care Program, spoke of ways and means to reduce unnecessary expenditures. They have had a reduction of funds, which necessitates a change in planning.

a. Dr. Silver also spoke about Family Planning and how the clinics are set up.

b. Dr. G. Bernard Shaw felt that both employees and physicians should be prorated with funds available.

IV. A short discussion on Rural Health Clinics and National Guidelines of Health Planning.

a. Various physicians throughout the County have been asked to act as contacts with the legislators in their districts.

V. Dr. James C. Bates stated that the fee schedule put out by Medicare did not cover night visits. He inquired, and found out that this would be taken care of, in the same way that Sunday and holiday visits were taken care of.

VI. It was voted to hold the next meeting at the Down East Community Hospital, Machias, Maine on Thursday, April 13, 1978 at 7:30 p.m.

KARL V. LARSON, M.D., *Secretary*

Androscoggin

The meeting of the Androscoggin County Medical Association was held at No Tomatoes in Auburn on January 19, 1978. The business meeting was preceded by a social hour and dinner. The business meeting was called to order by the President, Dr. Jou S. Tchao, with 64 members and two guests present.

The minutes of the December meeting of the Corporators were read and accepted as corrected.

Drs. Joel Olstein and August Valenti were voted to membership in the County Society and the Maine Medical Association.

Dr. Tchao reviewed correspondence from Dr. Wesley J. English, the secretary of Cumberland County Medical Society, regarding the Medico-Legal Panel to be held February 16 at Red Coach Grill in South Portland. Dr. Tchao urged all members to attend if possible.

Dr. Tchao announced the appointments to various committees, and a copy will be given each member.

Dr. Frederick C. Holler was substitute for Dr. Charles W. Steele to the State Insurance Committee meeting held in Brunswick. Dr. Holler gave a detailed report of the discussions and findings of the meeting. Most information was about finance of medical care and Blue Cross-Blue Shield problems and proposals.

Dr. Thomas F. Shields spoke of final plans for the Negotiations Seminar to be held at Ramada Inn, April 1 and 2. Registration is limited to 30. Application forms are in the mail at present; any member who hasn't one and desires one may obtain one from Dr. Shields or from Juliette Giguere, the assistant secretary.

Dr. Tchao introduced Dr. John Steeves, the chairman of the Political Action Committee of Maine Medical Association, who spoke of the duties and responsibilities of the committee. A question and answer period followed.

Mention was made of the assistance given us by Senators O. Snowe and Thomas Mangan on issues of Health Care. Dr. Richard M. Swengel moved that the Society express their appreciation for their support. The motion was seconded by Dr. Holler and duly voted. The secretary is to send a letter of appreciation.

Dr. Tchao introduced Senator Olympia Snowe who spoke of the various health care issues already being considered by Legislators. Her talk was followed by a lively question and answer period.

Dr. Tchao thanked both Dr. Steeves and Senator Snowe for their presentations.

The next meeting will be February 16, 1978 at No Tomatoes.

KENNETH P. WOLF, M.D., *Secretary*

Annual Meeting Dates For Your 1978 Calendar . . .

Maine Medical Association, June 10-13
Treadway-Samoset, Rockport, Maine

American Medical Association, June 17-22
St. Louis

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Control or Confusion?

Hospital Employee Tuberculosis Surveillance

GEORGE W. WOOD, III, M.D.*

A regular tuberculin testing program has been an integral part of hospital employee tuberculosis surveillance efforts for years. Such a program is designed to perform three functions: (1) detect "active" tuberculosis at a relatively early stage; (2) identify problems of tuberculosis control within the hospital; (3) select those individuals who should be offered chemoprophylaxis. Effective surveillance has become an evermore pressing need as sanatoria have closed and the responsibility for management of a tuberculous individual has shifted to physicians in the community hospitals and various ambulatory care facilities.

Through efforts of the Maine Lung Association and the State Department of Health, the remaining Maine Sanatorium was closed in 1971. Since that time, patients in northern Maine have been hospitalized at Eastern Maine Medical Center in Bangor when necessary. During the first year (1971-72), there were 35 admissions with sputum positive tuberculosis. In succeeding years, the number has rapidly decreased so that in 1976 only 15 people required hospitalization for this disease at the Eastern Maine Medical Center. Maine's one million population had an incidence of 6.9 per hundred thousand in the latter year.

This report summarizes the results of the first five years of the surveillance program at Eastern Maine Medical Center; expresses concern about its effectiveness; and suggests modifications.

MATERIALS AND METHODS

A supervised tuberculin testing program was implemented at Eastern Maine Medical Center in late 1971. In each of the years 1972, 1973 and 1974, a different nurse was responsible for the Tine® testing. However, during 1975 and 1976, one very conscientious nurse has been administering and measuring the Tine and intermediate PPD. Since September 1973, only Tween-80 stabilized PPD manufactured by one company has been used.

Employees are required to have an initial Tine test (Lederle-OT) and if negative it is repeated yearly. Those individuals with doubtful Tine results have an intermediate PPD (IPPD). The rare individual with a vesiculation response is considered positive and usually does not have a mantoux. If the employee has had a positive tuberculin test prior to employment, we have in most instances not repeated it but performed a chest x-ray instead. During the 1971-1976 interval, the number of employees has increased from approximately 350 to more than 1300. The tuberculin testing has been well received.

RESULTS

The percentage of new employees with a positive tuberculin test prior to employment has been as follows: 1972, 10%; 1973, 8.6%; 1974, 5.8%; 1975, 6.8% and 1976, 5% (Table 1). These figures include those who reported their test to have been positive in the past and may not have been retested at the time of employment. The conversion rates have been as follows: 1972, 2.6%; 1973, 0%; 1974, 0% and 1975, 2.5% (Table 1). The 1972-1974 figures represent the testing of 300-350 persons per year while in 1975 the number was somewhat more than 600.

The nineteen (2.5%) converters in 1975 had a mean induration of 16.2+/-4.6 mm; 84% had 2 or more yearly Tine tests prior to the IPPD. During 1976, the 3.4% converting had an average reaction size of 11.5+/-4.2 mm; 80% had 2 or more pre 1976 Tine tests. There was no particular job predilection noted among the converters. In the 1976 group,

*Courtesy Staff, Department of Medicine, Eastern Maine Medical Center, Bangor, Maine 04401.

Table 1

Tuberculin Reactor Rates Among Hospital Employees in Selected Institutions

Initial Test Positive or Previous "known" Positive		*% Conversion*	*Type Test*
Eastern Maine Medical Center			Tine or Tine & PPD (5TU)
1972	10 %	2.6	
1973	8.6	0	
1974	5.8	0	
1975	6.8	2.5	
1976	4.0	3.4	
RILEY			
1963	—	2.3	?
ATUK			
1968	13.6		PPD (5TU)
1969	16.0	1.9	
(Contacts of unsuspected TB		6.6)	
CRAVEN			
1972-73		0.25	PPD (5TU)
(Contacts of unsuspected		1.6)	
ARIZONA			
1972	7.1	3.5	?
RUBEN			
1973 Initl. Pos.	11.0	7.7	PPD (5TU)
"known" Pos.	5.2	(4.5-0 to ≥ 10m)	
		(3.2-± to ≥ 10m)	

there was a single case of active pulmonary tuberculosis. He was an old employee already being evaluated by his family internist because of respiratory symptoms. A sputum was negative on smear but positive on culture for M. Tuberculosis. Review of earlier chest x-rays suggested that this 62-year-old male from the housekeeping department had had a pre-existing area of linear fibrosis in the right upper lobe. The Tine had been reported "negative" in 1972, 73, 74 and 75. It was 3. mm in 1976 and the IPPD was 10 mm. Initial chest x-rays on all the other "converters" were negative as have been their follow-up films one year later. INH prophylaxis has been poorly received and maintained; the precise numbers are unknown.

There have been three instances of hospitalized patients whose active tuberculosis was not identified for several days or only upon their demise. The converters, however, were not among those personnel with known direct or indirect exposure to these patients.

Discussion

What does this experience mean? It is very simple — Employees at Eastern Maine Medical Center during the last two years are having an increasing exposure to active tuberculosis and therefore the rate of tuberculin conversion is increasing? Riley[1] notes, "Inasmuch as a single tubercle bacillus implanted on lung tissue of a tuberculin negative person is all that is required to infect, the hazard of infection depends on the likelihood that such an implantation will take place." To reduce this likelihood, the adequacy of room ventilation in the infectious disease unit at Eastern Maine Medical Center is assured by measuring air exchanges per hour at six- to twelve-month intervals. There has also been an emphasis upon cough education of the patient with suspected tuberculosis to assist in controlling dispersal of airborne infectious particles.[2-7]

How does this Center's reactor rate compare with other hospitals past and present? In the select student nurse population, the reactor rate is reassuring. During the last seven years at Eastern Maine Medical Center, 3% of 231 student nurses had a positive IPPD as entering freshmen in the three-year diploma school; a total of 0.8% have converted (Table 2). Weiss[8] describes the changing incidences of tuberculosis in student nurses at Philadelphia General Hospital from 1935 through 1971. In the earlier years, 28% of students reacted to one TU PPD on admission to the training program and at the end of three years, 100% reacted. By 1971, 4.8% of the students were reactive on entry and in three years only 1.6% converted. The average for the last 10 years was 4.1% on admission and 4.2% conversion by class. Levine,[9] reporting on 1,791 student nurses tested from 1948 to 1964, found the conversion rate of 66% in three years (1948-1951) had dropped to a rate of 3.5% by the class of 1964.

Table 1 compares the results of five hospital employee testing programs with those of Eastern Maine Medical Center. Atuk and Hunt[10] initiated an employee tuberculin testing program in 1968 and 1969 with a positive IPPD of 13.6% and 16% respectively. The conversion rate in 1969 was 1.9% of the total employee population and 6.6% in 225 employees who had close contact with "open tuberculosis within the hospital." They report that in the newly converted group 50% of those receiving one year of INH reverted to negative. The precise time interval between tuberculin tests is not stated. From the same hospital, Craven, et al[11] has reported results of tuberculosis surveillance in a 15-month

Table 2

Tuberculin Reactor Rates Among Nursing Students in Selected Institutions

Initial Test Positive or Previous "known" Positive		*% Conversion*	*Type Test*
Eastern Maine Medical Center			Tine or Tine & PPD (5TU)
Total in 7 years	3.0%	.08	
WEISS			
1971	4.8	1.6 in 3 yrs.	PPD (5TU)
LEVINE			
1964	5.3 (avg. 1959-64)	3.5 in 3 yrs.	PPD (5TU)

period in which hospital personnel and student nurses were exposed to 17 individuals with unsuspected tuberculosis. Fifteen were in-patients and 2 out-patients. Three (3.1%) of 95 students and five (1.3%) of 389 personnel or a total of 1.6% converted. During the same period, 0.5% of 2,013 non-exposed personnel converted. The authors do not define their criteria for conversion but do note that 10 mm or more of induration is considered "positive."

The problem of the unsuspected tuberculosis patient was described by Ehrenkranz and Kicklighter.[12] Among 100 tuberculin negative hospital personnel exposed to a highly infectious patient with autopsy documented caseating bronchopneumonia 23 converted. In most, the pre-exposure test was an OT Tine test whereas all had IPPD post exposure. Ten persons had little or no direct contact with the patient and were thought to have been infected due to a poor ventilation system. The authors do not comment regarding the conversion rate of employees in other parts of the hospital.

When the state of Arizona initiated the use of the general hospital for tuberculosis care, tuberculin testing of employees was required of those participating institutions.[13] The initial tests of 8,066 individuals produced a reactor rate of 7.1%. Repeat skin tests of 6,274 employees were performed six and twelve months after the first test with the conversion rate of 3.5%. The testing method is not stated. Only five of the converters had known exposure to tuberculous patients so the authors assumed the remainder had been exposed to individuals with unrecognized disease in or out of the hospital environment.

Recently Ruben and colleagues[14] reported the experience of a 450-bed hospital in Pennsylvania who started their surveillance program in 1973. Intermediate PPD was used in testing 80% of approximately 1500 employees. Eleven percent had induration > 10 mm, and 5.2% were previously known positive. At six- and twelve-month intervals, repeat skin tests were offered. Thirty-one months after the initiation of the surveillance a total of 626 (42%) employees had received two or more tests. Twenty-eight (4.5%) changed from 0 reactivity to 10 mm or greater while 20 (3.2%) increased induration by 6 mm or more on their first response of 3-9 mm. There was a tendency for old employees to constitute the latter group. Six (1%) employees increased reactivity by less than 6 mm. Interestingly, the individuals with a high degree of exposure had a lesser conversion rate than those with a low degree of exposure. The difference is ascribed to "the high incidence in housekeeping personnel." No medical or nursing students were involved in the study. There was no x-ray evidence of pulmonary tuberculosis in the converters and the acceptance of INH prophylaxis was limited, particularly in older individuals. The investigators thought those with initial reactivity who converted may represent examples of the "booster effect" of the first test.

It is this "boosting" question which seems most perplexing and was noted as one of the special problems in identifying true converters by the Committee on Diagnostic Skin Testing of the American Thoracic Society.[15] Several earlier studies by Tukey, et al[16] using first and second strength PPD for multiple testing of nursing students led to their concluding that there was "no evidence of an increase in sensitivity due to tuberculin testing, although a small increase (or small decrease) in sensitivity from this cause might pass undetected." Some of the students were tested as many as 22 times with multiple strengths in three years. The significance of the use of non-stabilized solutions and the first and second strength material rather than the intermediate dose is unknown. Smith and Johnston[17] commenting on this paper and their own experience suggested that the danger of mistaking the "booster effect" could be avoided by retesting with second strength PPD those individuals who were non-reactors to 5 TU. By their reasoning, those not reacting to 100 TU (? second strength) if positive at a later date, would represent new tuberculous infection. In a hospital employee surveillance program, this would not seem to be a practical solution. The "booster effect" is seen more often in older individuals as their fading reactivity is rejuvenated by repeated skin tests. However, age cannot be *the* deciding factor. Sometimes resolution of the problem of conversion or "boosting" is assisted by the presence of calcifications on previous chest x-rays as reported by Duboczy[18] and noted in the one employee with active tuberculosis detected at Eastern Maine Medical Center.

One of the most impressive demonstrations of

"booster effect" is a series of studies by Ferebee and Mount.[19] They found in three institutionalized groups that 15-25% changed their IPPD from less than 8 mm in the initial to more than 8 mm in the second test one year later. No active tuberculosis was identified in their groups. To pursue this problem, two other hospital populations were retested three and six months after an initial IPPD. Forty-three percent converted in three months and 28% in six months; seemingly the shorter the interval between tests, the higher the rates of "conversion." This incongruity led to the third phase of the study as they sought to determine the time in which the "booster effect" might first appear. A series of tests with PPD and diluent at one- to five-week intervals was administered. The effect was evident by the first week with generally little further increase after the second test. There was, however, a tendency for reactions between two and ten mm on the second test to become larger on the third. None which increased in size between the first or second test reverted to their previous size on the third. It was their opinion that this phenomena was due neither to sensitization of the individual by the tuberculin solution nor evidence of new infection but only a waning sensitivity related possibly to age and time since the original infection. Comstock elaborated somewhat on this anamnestic premise in his discussion of false tuberculin test results.[20]

In 1969, Raj Narin[21] presented the results of repeat testing with 1 TU PPD in Indian villages. Retesting was done at 2 months in one group and 18 months in another. The conversion rate was greater at 2 months than at 18. In those people age 15-24 years, 44% had reactions > 8 mm after the shorter interval, while during the longer interval 26% became positive by this criteria. If induration was ≥ 14 mm, the figures were 27 and 13%. He felt, "it is highly improbable that the actual rate of infection was greater during the shorter period than the longer period." The increase in induration was more marked in those with an initial intermediate reaction. It was also more apparent with an increase in age. The author concluded from this and other data that in the population under study with "widespread prevalence of non-specific allergy" an increase of 16 mm on retesting was necessary before it is considered evidence of new tuberculous infection.

Glassroth[22] gave a preliminary report of the Center for Disease Control study on "boosting" at the May 1977 American Thoracic Society meeting in San Francisco. A population of 1,521 individuals received 5 TU of PPD-T; 70% also received 5 TU of PPD-G. At 2 and 7 days the PPD-T was repeated. "Boosting," an increase of induration > 6 mm and a change from less than 10 to greater than 10 mm occurred in 2.1% of those who had 0 initial reaction and 9.1% of those with > 0 reaction. Those volunteers under age 35 boosted in 1.8% of the instances and those over 35 in 5.5%. The authors thought non-tuberculous mycobacterial sensitivity might be the most common cause of "boosting."

Instead of being primarily concerned with "booster effect" Katz and Associates[23] investigated both the increase and decrease in sensitivity to tuberculin in 25,000 school children using the Heaf Tine test. Approximately one-third were tested yearly, the others less frequently. This test material contains a relatively large dose of tuberculin which may increase the possibility of cross reactions to "atypical" mycobacterial infection. The authors note, however, that for the purpose of comparing variation in sensitivity this was not considered significant. Changes were most often in those with mild reactivity but occurred in all gradations. This was demonstrated in a subset of 9,188 people originally having a "negative" reaction of 0-3 nodules. Six percent of those with 0 nodules originally, converted to 4 or more (positive). In contrast, 25% with 1-3 nodules increased to 4 or more. In the total, subset reversions to 0-3 nodules occurred in approximately 50% of reactors who originally had 4 nodules. Time intervals of one to four years apparently influenced the rate of change relatively little. The authors felt "variation in sensitivity was the rule rather than the exception."

The problem of conversion-reversion was demonstrated in the work of Furcolow, et al.[24] In administering PPD-S, they found that the conversion rate from kindergarten to first grade was roughly three times the predicted and that a majority of the positive tuberculin reactors were in the 5-9 mm range initially.

One part of the program involved testing the same group of students in the 8th and again in the 9th grade. Investigation of those first found positive to the test in the 8th grade revealed 5% of the students had contact with known tuberculosis cases. The same type of investigation of the students converting between the 8th and 9th grade identified known tuberculosis in only 0.8% of their contacts. Based on their data obtained during an unpublished three-year study, they state "that the frequency of conversion and reversion of both tuberculin and histoplasim skin tests was related to the frequency of retesting. Thus, at six months the tuberculin conversion rate was 6% and the reversion rate almost 35% whereas at three years retest the conversion rate was 0.8% and the reversion rate 7.6%.

Seeking other ways to define individuals infected with M. Tuberculosis, Edwards, Acquaviva and Livesay,[25] in addition to measuring induration, used Palmer's method of determining reaction density. The method is of limited value.

The extent to which many of the earlier studies were materially influenced by the use of non-stabilized tuberculin solutions is unknown. The phenomena of absorption by the container or syringe has been reported by many investigators. Landi, Held and Tseng[26] utilizing tuberculin purified protein derivative-^{14}C found the non-stabilized solu-

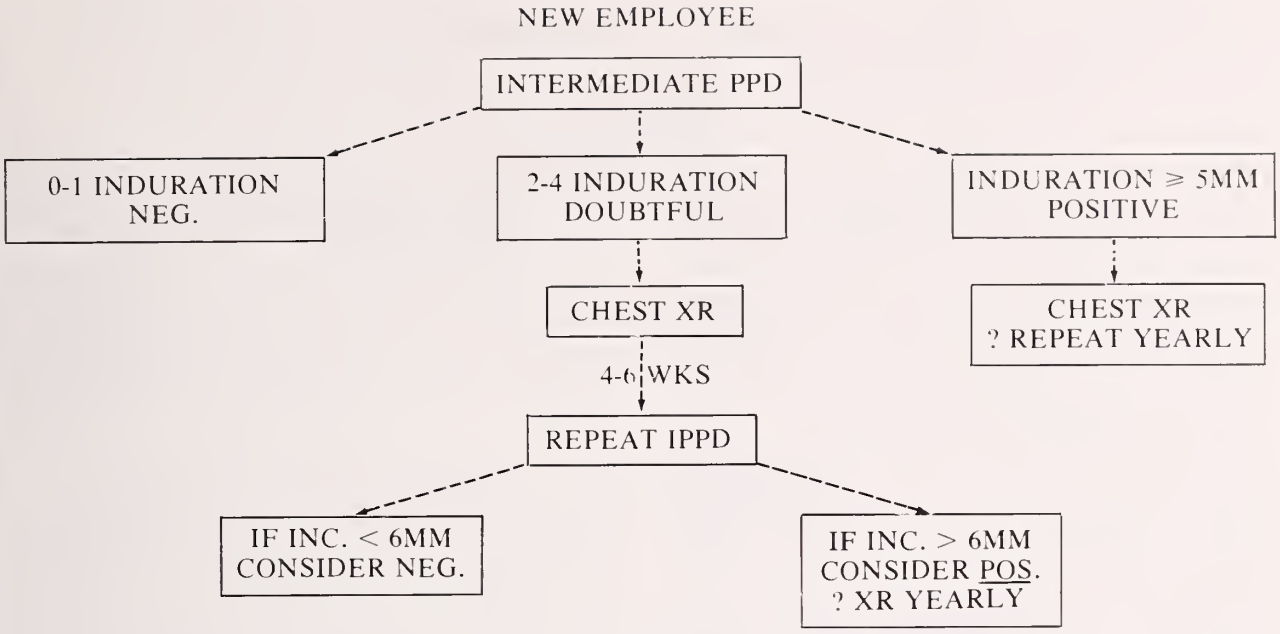

Fig. 1

tion lost 40% of its original concentration in 24 hours. It decreased further in plastic syringes, e.g., at one hour only 30% of the original potency remained. Stabilized solutions lost none throughout the total 24-hour time of the study.

Purification of tuberculin antigens may lead to skin tests of greater specificity in identifying those infected with mycobacteria.[27] The mycobacteria contain both species specific and non-specific antigens. Perhaps the identification of specific cellular components related to hypersensitivity and immunity may lead to the sophisticated serological identification of substances produced in response to infection with M. Tuberculosis.[28,29] Until that day arrives how shall we deal with the present conundrum?

The Ad Hoc Committee of the Scientific Assembly in their statement of February 1977 on screening for tuberculosis in institutions partially approached the problem.[30] Their decision applied to patients, children, and inmates in various institutions but unfortunately do not outline a program for employees.

Conclusions

For many years I have been a "true believer" in the reliability of the tuberculin skin test. Doubts were slow to come but now I am possessed by them. Simply stated — the tuberculin skin test has broad limitations as a diagnostic and epidemiologic tool. Reactions wax and wane impressively for reasons which are unknown. True, this is seen more often in and after the "middle years" but school children are not exempt. The varying sensitivity may be apparent after a few days and may last for years. It is manifest in a few who initially have no reaction but in the vast majority of reverters-converters, some response is initially noted. It has been repeatedly suggested that exposure to unclassified (atypical) mycobacteria may affect the sensitivity to IPPD. The change of > 6 mm with induration > 10 mm to identify converters as recommended by the American Thoracic Society, may be the best we can do. We will have to live with the uncertainty but reality demands a decision in hospital tuberculosis surveillance programs.

In answer to this problem I would like to propose the following: One, discontinue use of the multiple puncture test. It introduces an uncertain quantity of tuberculin material but more importantly enhances the potential for an increased incidence of "boosting" in the sequence of the *doubtful Tine followed by the IPPD*.

Second, introduce a program using the intermediate strength PPD in a somewhat different fashion (Fig. 1). All new employees regardless of history of previous positive tuberculin would have an IPPD. This would recognize the unreliability of individual's recall of their previous tuberculin test results. Reichman and O'Day[31] have recently documented this fallibility. If no induration is present, no further testing would ensue unless an individual was exposed to a non-isolated patient with active pulmonary tuberculosis (Fig. 2).

An individual with an initial reaction of greater than or equal to 5 mm is x-rayed at that time and (?) yearly thereafter. Because recognized infection with unclassified mycobacteria is so rare in *Maine, ≥ 5 mm induration is considered positive.*

If a new employee has a 1-4 mm of induration, a chest x-ray is done and a second IPPD is administered in four weeks in order for any probable "booster effect" to make itself known. Changes in induration <6 mm would require no further study and this individual would be considered as a negative reac-

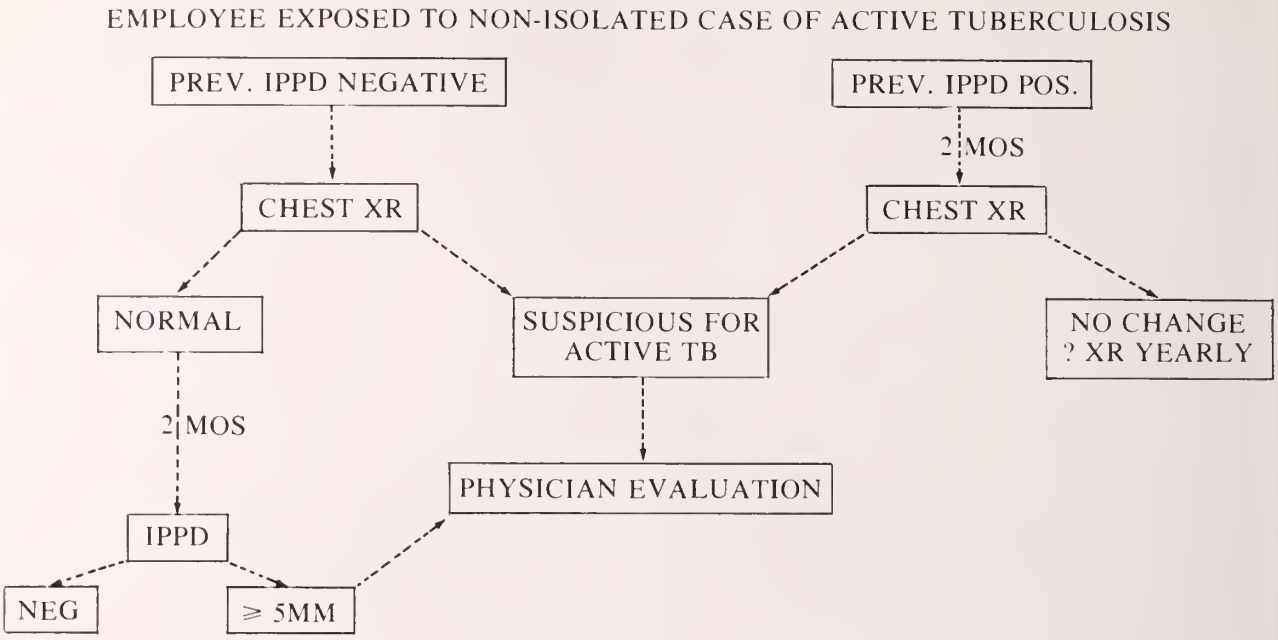

Fig. 2

tor. Those with an increase > 6 mm may have yearly chest x-rays.

The only other circumstance under which an employee is skin tested is upon exposure to a non-isolated patient with sputum positive pulmonary tuberculosis (Fig. 2). If the employee's PPD had previously been negative, a chest x-ray is done. Those with x-rays suspicious for tuberculosis are referred to a physician without further testing by the Employee Health Service. If the x-ray is normal, a PPD is done in two to three months. This will avoid the potential of "boosting" present in the close sequence of tests done two to three months apart. If this PPD is negative, the evaluation is complete. If it is ≥ 5 mm, he is referred to a physician. The employee whose pre-employment IPPD was ≥ 5 mm may or may not have a chest x-ray in two to three months. If no change is noted from the original film, further action is unnecessary. If there is suspicion of active tuberculosis, he is referred to a physician. Throughout the program, decisions on INH chemoprophylaxis will be made on an individual basis.

This total plan will permit more accurate identification of the new employees' tuberculin status and will help avoid the labeling of individuals as converters who manifest "boosting." The number of individuals placed on INH chemoprophylaxis will be less, thus reducing the risk of adverse drug reactions.

The alternatives to the above program could be: One, to abandon all routine tuberculin testing of employees and request individuals developing certain symptoms or signs to report to an employee health office; or two, do a single intermediate strength PPD as part of a pre-employment exam and then request return for symptoms and signs only. Both of these alternatives are less attractive at the moment in that they would lead to a complacent attitude toward tuberculosis identification and control in employees *and patients*.

Hospital employee tuberculosis surveillance programs should lead to control — not confusion. I await that time.

Acknowledgment

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Treatment of Acute Leukemia in Adults

DELVYN C. CASE, JR., M.D.*

Acute lymphoblastic leukemia (A.L.L.) in children has changed from a uniformly fatal disorder to a curable disease. In most series, 90-95% of all children achieve a complete remission and more than 50% are still in remission after 5 years.[1] While the results with acute leukemia in adults have not been as spectacular, significant advances have been made. In this paper, the progress in treatment and care of acute leukemia in adults will be reviewed.

ACUTE MYELOGENOUS LEUKEMIA

Eighty-seven percent of acute leukemia in adults is of the myeloid type. This is a heterogenous group of disorders consisting of acute myeloblastic leukemia (A.M.L.) (63%), acute myelomonocytic leukemia (A.M.Mo.L.) (18%), acute monoblastic leukemia (A.Mo.L.) (10%), erythroleukemia (E.L.) (5%), and acute promyelocytic leukemia (A.P.L.) (4%). Each of these types presents different clinical challenges. A.M.L. and A.M.Mo.L. are usually thought to be the prototype disorders of the group with equivalent clinical features and remission rates. One series, however, suggested that survival in A.M.Mo.L. is twice that seen for A.M.L.[2] A.Mo.L. is more sensitive to therapy, but relapses occur sooner. This type of leukemia may also demonstrate lymphoid characteristics and, therefore, respond to prednisone and vincristine.[3] A.P.L. and E.L. have been notably resistant to chemotherapy; however, since the introduction of daunorubicin (an investigational drug), responses are expected and remissions durable.[4,5] A.P.L. is also characterized by a high incidence of disseminated intravascular coagulation (D.I.C.) also seen occasionally in A.M.Mo.L.[6,7,8]

Remission-induction of A.L.L. in children has almost become an outpatient procedure because of the specificity of the drugs for lymphoid cells and the relative lack of myelosuppression by prednisone and vincristine. In adults, the treatment of acute leukemia produces severe bone marrow suppression because of the relative lack of specificity of leukemic and normal cells to the cytotoxic effects of the drugs. Suppression of red cell and platelet production require transfusions. Severe myelosuppression requires great care in the treatment of infection and possible use of granulocyte transfusions. Platelet counts usually reach 1000-10,000/mm.[3] Granulocytes often reach a nadir of 50-500 neutrophils/mm.[3]

Complete remissions have been attained in a minority of patients treated with single agents: 6-mercaptopurine (15%), 6-thioguanine (6-T.G.) (20%), and cytosine arabinoside (Ara-C) (25-39%). Ara-C and 6-T.G. in combination regularly produces remissions in 50-60% of patients.[9] Similar data are obtained with the C.O.A.P. regimen (cyclophosphomide, vincristine (Oncovin®), cytosine arabinoside (Ara-C), and prednisone).[10] The most significant new drug available is daunorubicin. Forty percent of patients achieve a complete remission when this drug is used alone. More importantly, in combination with Ara-C (given by continuous infusion over 7 days), 65-75% achieve a complete remission.[1,2] In one recent series, 80% of patients treated with 6-T.G., Ara-C and Daunorubicin went into complete remission.[11] Age is often the most important clinical characteristic bearing upon response to treatment and survival. However, in patients older than 60, intensive therapy is still advantageous with 55% obtaining a complete remission.[1]

The daunorubicin/Ara-C protocol is being used at the Maine Medical Center. Since July of 1976, 11/13 (85%) of patients have achieved a complete remission[12] — results quite comparable to other centers.

The duration of remission is still disappointingly short. The median duration of remission in acute leukemia of adults is only 12 months with median survival of 24 months. Importantly, however, 25% of patients are still in remission after five years.[9] The short remission duration is probably related to the relatively few effective drugs available for adequate maintenance programs.[13]

One approach to this problem of relapse is "late intensification" — using aggressive remission-induction style therapy during the maintenance phase. Initial results are encouraging.[14] Another approach has been immunotherapy. Early results with B.C.G.[15] have not been duplicated. However, in a study injecting neuraminadase-treated leukemic cells and the methanol-extracted residue of B.C.G. into leukemic patients in remission, the median duration of remission has been extended to 36 months with survival doubled over that obtained with chemotherapy alone.[1]

BLASTIC CHRONIC MYELOGENOUS LEUKEMIA (C.M.L.)

C.M.L. comprises 20% of leukemia in adults. Usually 80-90% of patients can be stabilized with oral busulfan for 1-4 years; blood counts may normalize but the Philadelphia chromosome (present in 90% of patients) persists. Even in the more aggressive treatment programs, only rarely has the Philadelphia chromosome been eradicated. In these cases, elimination of the chromosome has been temporary and without benefit to survival.

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In most cases, blast crisis supervenes. This phase is refractory to most chemotherapy, and only 10% of patients achieve a remission.[16] Interestingly, in 25% of patients with blast crisis, the blast cells appear to be lymphoblastic in morphology.[17] When these cells are assayed for a lymphoid marker, terminal deoxynucleotidyl transferase, they are frequently positive.[18] In these patients, stabilization of disease and prolongation of survival have been achieved with prednisone and vincristine compared with results achieved with a myeloid leukemia regimen. At the Maine Medical Center, we have been using the C.O.A.P. regimen (cyclophosphomide, vincristine (Oncovin), cytosine arabinoside (Ara-C), and prednisone) in these patients. It is too early to evaluate any advantage for this group of patients treated with this regimen that combines A.L.L. and A.M.L. therapy. Specimens for terminal deoxynucleotidyl transferase are being sent to collaborators for analysis.

Acute Lymphoblastic Leukemia (A.L.L.)

A.L.L. comprises only 13% of acute leukemia in adults. Results with therapy have not been as encouraging as in children. While age may be a factor in response, the morphologic heterogenity of the blast cells in adults with A.L.L. may reflect differences in cellular origin, metabolism, or kinetics[6] that directly relate to sensitivity to chemotherapy. With A.L.L. regimens, 80% of adults obtain a complete remission; but median duration of remission and survival are only 25 months and 32 months respectively.[19]

Preleukemic Syndromes

A number of syndromes including sideroblastic anemia, refractory anemia with increased blasts, paroxysmal nocturnal hemoglobinuria, and chronic myelomonocytic leukemia can terminate in acute leukemia.[6] Often a diagnosis of "preleukemia" is suspected in these patients; but a diagnosis can often only be made when acute leukemia develops. Early leukemic treatment has not been found to be advantageous. Once leukemia has developed, treatment can be equally effective as with *de novo* leukemia.[20]

Supportive Measures

Therapy for adult acute leukemia causes severe bone marrow suppression. Many early deaths occur. Impairment of megakaryocyte development and platelet function produce extremely low platelet counts and bleeding. Vigorous transfusion of platelets are required when counts dip below 10,000-20,000/mm,[3] and/or signs of bleeding develop. Transfusions of red cells are required to keep the hematocrit 25-30%. Hemorrhage from thrombocytopenia is more likely to occur with very severe anemia. Heparin has to be applied early in cases of A.P.L. because of the high incidence of D.I.C.

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Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCl and/or clidinium Br

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants, and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Physical and psychological dependence rarely reported on recommended doses, but use caution in administering Librium® (chlordiazepoxide HCl) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) reported following discontinuation of the drug.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy. Advise patients to discuss therapy if they intend to or do become pregnant.**

As with all anticholinergics, inhibition of lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established.

Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated; avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment, blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, *i.e.*, dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

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PATIENT PACKAGE INSERTS: A CONCEPT WHOSE TIME HAS COME?

The consumer's right to know is an irreversible and desirable trend of the Seventies. It extends, and properly, to a patient's right to know more about his or her prescription medications. One way, gaining favor, is through patient package inserts. Wisely-prepared and properly distributed when medically indicated, they could markedly improve patient knowledge and drug therapy—laudable goals by anyone's standards.

The PMA endorses these goals and will work with government, the health professions and consumers to achieve them.

The Advantages

The concept holds promise of benefits: better patient understanding of the product prescribed, better adherence to the treatment plan, and more awareness of possible side reactions.

Every doctor has had patients who fail to finish antibiotic regimens because they feel better. Some patients assume that if one tranquilizer or analgesic is good, two may be twice as good. Still others fail to report dizziness while on antihypertensive therapy —and so on.

Problems like these might arise less often if the patient received written information in addition to verbal instructions. Some studies suggest that patients are more receptive to such materials, and they more often understand the verbal instructions and follow them, when inserts are used.

The Disadvantages

There are also some potential problems. Obviously, the inserts must be clearly phrased, without extraneous or complex detail. How much information is enough? How can it be kept current? Should all patients receive the same information? Should inserts be included with all drugs? Should only potential problems be listed or are patients better off with a "fair balance" presentation that describes usefulness as well as drawbacks?

These and similar questions require answers, since model inserts have yet to be properly developed and tested. Despite the need for these studies, the FDA is proceeding prematurely with inserts on selected products. We think the Congress is the only place where the matter can be given the proper legal status and direction, particularly since it represents a conceptual change in the legal, medical and social framework of the nation's prescription drug information system.

The Solution

The PMA believes that carefully-devised pilot studies of various kinds of inserts are needed. They should be developed and implemented with full participation by doctors, pharmacists, consumers, communications experts and the drug industry. Such studies will provide reliable pathways to follow, so that inserts will be useful aids to medical practice.

And particularly we think that you should be closely involved in this debate and in these studies and decisions. Otherwise, people with less experience and qualifications may control the purposes, content and use of a tool with considerable promise for improved patient care. It could make a difference in your practice tomorrow, and more importantly, in the health of your patients.

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which can be greatly exacerbated by the initiation of treatment.[4,6]

Infection is currently the most common cause of death. Sophisticated bacteriologic laboratory facilities are necessary along with prompt application of broad-spectrum antibiotics in patients with suspected sepsis. Undefined pneumonias and other lesions should be considered for biopsy early. Although broad-spectrum antibiotics are often lifesaving, many patients with severe neutropenia are unable to contain infection and develop fatal infectious complications. A new approach to this problem has been granulocyte transfusions. Recent reports have shown significant improvement in mortality in patients receiving granulocytes versus those patients receiving antibiotics alone.[21,22] Granulocyte transfusions are now being used at Maine Medical Center in patients with severe neutropenia. It is hoped that granulocyte transfusions might decrease the morbidity and mortality associated with infection during remission-induction therapy.

Pneumocystis carinii pneumonia plays a prominent role as an opportunistic infection in the compromised host. Treatment with trimethoprim-sulfamethoxazole has been shown to be as effective as pentaminidine without the side effects associated with its use.[23] Recently, trimethoprim-sulfamethoxazole has also been shown efficacious in preventing infection with pneumocystis when given prophylactically during chemotherapy.[24]

Future Prospects

Although progress in treatment of adult acute leukemia has been made, results have lagged behind the successes obtained with childhood acute leukemia. With combination chemotherapy especially daunorubicin and cytosine arabinoside, 70-80% of adult patients should achieve a complete remission. Further clinical research is necessary to develop new drugs for induction of remission, and especially for more successful maintenance programs. When patients relapse, chemotherapy may produce a second remission; but this remission lasts only four months.[9] Late intensifications[13] and/or immunotherapy[1] may play roles in future treatment protocols. 5-azacytidine is a new drug that has shown great promise in patients with refractory leukemia and has been suggested as an additional drug during induction remission.[25,26] The severe nausea and vomiting produced by the drug has limited clinical trials. Bone marrow transplantation has demonstrated efficacy for a small but definite percentage of patients (15%) with acute leukemia resistant to conventional treatment.[27] Eradication of the refractory leukemic population of cells, sensitization to transfused blood products, and graft-versus-host disease remain as serious technical and clinical problems.

Exact characterization of blast cells,[6,28] an understanding of *in vitro* growth patterns of leukemic and normal cells,[29] and determination of the labelling index as a measure of generation time of cell growth,[30] may play roles in understanding the leukemic process and in selection of agents more specific for leukemic cells.

Remission induction demands meticulous and aggressive care during the period of severe bone marrow suppression. Infection is currently the most significant problem. Granulocyte transfusions may play a more important part in future treatment programs. Lithium carbonate has been shown to produce leukocytosis in patients treated for manic depression; it has been shown to attenuate the bone marrow suppression of chemotherapeutic agents.[31,32,33] Its possible role in leukemia could be promising. To prevent infection, the use of nonabsorbable antibiotics[34] and laminar flow isolation[35] are actively being explored. The promise of preventing pneumocystis pneumonia with trimethoprim-sulfamethoxazole might encourage the development of other agents that could prevent serious infection by the common pathogens.

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Continued on Page 128

Angiodysplasia of the Cecum

A Case Presentation

James W. Georgitis, M.D.,* L. Reed Altemus, M.D.,**
Louis N. Taxiarchis, M.D.*** and Walter B. Goldfarb, M.D.†

Angiodysplasia of the cecum is a rare disorder of arteriovenous malfunction which can be preoperatively defined by arteriography. It frequently presents as a diagnostic and therapeutic dilemma of lower gastrointestinal bleeding. Because vascular lesions of the gastrointestinal tract are rare and diverticulosis common, the problem becomes more complex in the patient with diverticulosis and bleeding. The case presented reflects this dilemma and has all the features of this supposedly rare disorder.

When organized approaches to lower gastrointestinal bleeding exclude esophageal varices, ulcer diathesis, diverticula, or carcinoma by routine radiological and endoscopic studies, additional procedures to define the site of bleeding are required. The percentage of cases of gastrointestinal bleeding that are undiagnosed range from 3 percent to 27 percent.[1,2] In fact all diagnostic procedures except selective arteriographic studies may fail to yield a diagnosis of angiodysplasia. When the diagnosis is made angiographically, the pathologist may fail to make the diagnosis because of the small area of involvement.

Case Report

An 80-year-old man was admitted to Maine Medical Center because of his fifth episode of rectal bleeding. His first admission, in 1974, revealed aortic stenosis, a thoracic aneurysm, bilateral inguinal hernae, diverticulosis of the colon, and a microcytic anemia. In 1975, rectal bleeding again occurred; and in addition, he had pneumonia. The usual radiological studies failed to define the site of bleeding. During 1976, he was admitted twice for rectal bleeding. During this admission, a question of duodenal ulcer was raised because of deformity of the duodenal bulb previously noted but dismissed because of negative gastric aspirates and normal esophagoduodenoscopy. Physical examination revealed an elderly man with a murmur of aortic stenosis, a thoracic aneurysm, bilateral inguinal hernae, and bleeding per rectum. A nasogastric aspirate was again free of blood. A gastrointestinal consultant felt that colonoscopy would not be successful because of the rate of rectal bleeding. He was transfused four units of blood, and the hematocrit rose from 27 to 39 percent. He then underwent sigmoidoscopy with visualization of the diverticula and blood from above the sigmoidoscope. Angiography was postponed because of the increasing hematocrit. The patient stabilized for four days in spite of a continuous "ooze"; therefore, a contrast B.E. was scheduled. An acute bleed again occurred on the eighth hospital day. Colonoscopy was obscured by blood. Selective angiography was performed revealing "vascular ectasia" of the right colon. Bleeding again stopped, and operative intervention was delayed because of increasing pulmonary failure and cardiac decompensation. In spite of the angiographic findings, the presence of extensive left sided diverticulosis caused a dilemma as to the appropriate operative procedure. The patient again bled heavily per rectum, forcing a decision. A subtotal colectomy was performed with ileorectal anastomosis associated with incidental splenectomy, gastrostomy, and repair of his inguinal hernae. The latter was prompted by fear of possible incarceration. His postoperative course was complicated by CHF and pulmonary failure. He developed acute cholecystitis with bacteremia postoperatively which responded to medical management. In spite of these complications, the patient sur-

Fig. 1. *Right Colon*: This low magnification of the mucosa demonstrates numerous dilated endothelial lined vascular spaces in the submucosa communicating with larger vascular channels whose walls contain smooth muscle and appear venous.

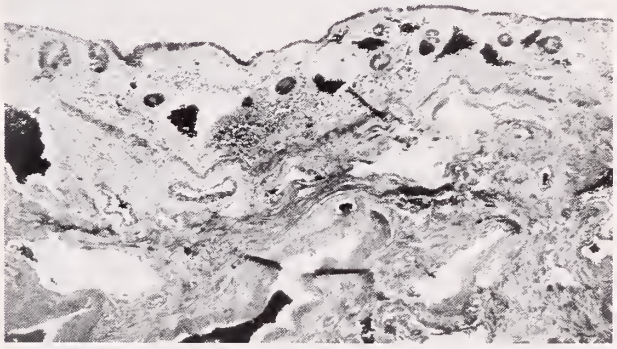

Fig. 2. *Right Colon*: This higher magnification, again, demonstrates the numerous mucosal and submucosal vascular channels of variable wall thickness.

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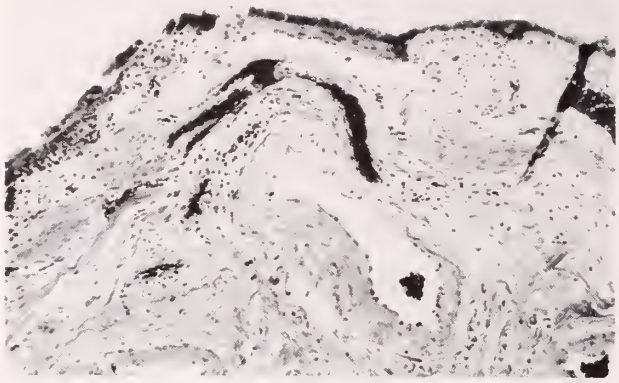

Fig. 3. *Right Colon*: This highest magnification demonstrates, again, a thin, dilated, endothelial lined channel which is continuous with a vessel whose wall reveals prominent smooth muscle fibers.

vived and was discharged one month from the date of admission. Follow up reveals the patient to be free of gastrointestinal bleeding. Gross examination of the surgical specimen revealed extensive diverticulosis of the descending and sigmoid colon. There was no evidence of an obvious bleeding site. An attempt was made to inject the vessels with barium, but failed. The bowel was then fixed in formalin overnight and re-examined. Again, no obvious mucosal abnormality was found; however, two small flattened areas with punctation were noted in the cecum measuring 6 mm. and 8 mm. in diameter. These were thought to represent Peyer's patches. Sections were taken through these areas as well as serially along the length of the bowel.

Microscopically, sections from these two sites revealed a flattened, but intact mucosa with an underlying vascular anomaly characterized by greatly dilated, thin walled, vascular channels communicating through the muscularis mucosa with larger vessels whose walls varied in thickness depending on the amount of smooth muscle. They resembled veins rather than arteries. In addition, a single small artery was found in the submucosa containing an atheromatous embolus. No evidence of an acute diverticulitis was found. A diagnosis of angiodysplasia was made.

Discussion

The first published case of gastrointestinal bleeding associated with arteriovenous malformation was by Gentry, Dockerty, and Claggett in 1949.[3] Baum was the first to clearly describe the radiological, clinical, and pathological correlation of colonic bleeding with arteriovenous malformation.[4,5] He named this disorder angiodysplasia to prevent the attachment of a congenital basis to its etiology. He also cautioned against ascribing all massive colonic bleeds to diverticular disease and supported attempts to define the exact site of bleeding by angiography.

The first study to show a relationship between aortic stenosis and lower gastrointestinal bleeding was by Williams in 1961. In a review of 1,443 cases of gastrointestinal bleeding at the Massachusetts General Hospital, he established a correlation of a higher incidence of gastrointestinal bleeding in patients with aortic stenosis than in the general population. The etiology was established in 93.5 percent of the cases. In the remaining 6.5 percent, no diagnosis was established. Aortic stenosis was present in 25.5 percent (24 of 95 patients) of these cases of undefined etiology of gastrointestinal bleeding. A matched control of age and sex showed that only 5.2 percent of the population had aortic stenosis.[6]

The common clinical features of angiodysplasia are arteriovenous malformations localized in the cecum in elderly patients, 60 years old or older, who commonly have aortic stenosis.[7] Usually multiple hospitalization have occurred for lower gastrointestinal bleeding which resolves acutely but remains recurrent.

The etiology of these lesions remains unknown. Hypotheses involving congenital malformation of vascular tissue of the cecum, ectasia of vessels from arteriovenous shunting in a chronic ischemic colon, and artherosclerotic embolic phenomena have been advanced. Congenital etiology for angiodysplasia is partially supported by the association of bicuspid aortic stenosis, a congenital disorder, rather than mitral stenosis, frequently a post infectious acquired valvular disease with angiodysplasia.[7] Congenital etiology is further supported by the association of arteriovenous malformation of the bowel with Maffucci's Syndrome (dyschondroplasia and haemangiomas).

Baum hypothesized that these areas of vascular ectasia result from arteriovenous shunting when transcient increase in intraluminal cecal pressure creates ischemia of the bowel wall. Ischemia occurs because wall tension occludes vessels as luminal diameter increases according to the Law of LaPlace (wall tension is directly related to the diameter of the lumen). However, these lesions are transmural, and the normal blood supply of the serosa, submucosa, and mucosa are formed from separate arteriovenous networks. If one accepts this hypothesis that vascular ectasia results from ischemic change, then it is easy to ascertain that the cecum should be the prime area of involvement because its larger lumen size allows more wall tension to develop and "maximum ischemia" to localize to this section of the bowel.[8]

An alternative hypothesis is that cholesterol emboli from an atherosclerotic aorta shower into this section of bowel, predispose to the development of ischemia, thus "fostering" the development of angiodysplasia. Possibly, local pooling of blood in congested venous channels behind cholesterol crystals precedes the development of these arteriovenous malformations.[9] However, the exact etiology of angiodysplasia still remains unclear.

The angiographic diagnosis of vascular ectasia of the cecum and ascending colon is recognized by visualizing clusters of small arteries along the antimesenteric border of the cecum and ascending colon, accumulation of contrast medium in vascular spaces, intense opacification of adjacent bowel wall, and early visualization of draining veins. Occasionally, active bleeding is suggested by identifying the presence of intraluminal contrast material. The actual arteriovenous malformation may vary from obvious to undetectable size. Magnification

Fig. 4A. Angiographic visualization of ectasia of the cecum: The arterial phase of the superior mesenteric arteriogram shows enlarged arteries to the cecum and proximal ascending colon. Contrast material accumulates within focal areas representing vascular spaces (arrows).

techniques are often helpful in defining smaller lesions. The angiographic detection of gastrointestinal bleeding usually requires an active bleeding rate of at least .5 mm. per minute. This is not necessarily a requirement for the visualization of vascular ectasia which depends only upon visualization of its submucosal component.

At Maine Medical Center, mesenteric angiography is selected prior to barium enema if the estimated rate of bleeding is greater than .5 ml. per minute. At less than this rate, colonoscopy as a diagnostic approach is feasible. The usual dilemma of too slow a bleed for angiography versus too fast for colonoscopy is resolved by the "rate calculator," the anxious surgeon who would rather define a source of bleeding than make multiple colostomies and risk infection in the patient.

Pathology may be at a loss to provide a diagnosis even with the appropriate specimen section. These small lesions may be indistinguishable from normal appearing mucosa. The excised specimen may be injected with silicone, Schlesiger's gelatin mass, methyl methacrylate, microfil, or barium by a vascular pedicle to help display the lesion. Care must be taken to ligate all vessels when the specimen is resected. Even then the mucosal surface may require inspection by both surgeon and pathologist to find these minute defects.

Once isolated, sectioned, and fixed, microscopic examination reveals multiple mucosal and submucosal "telangiectasia." Multiple arteriovenous channels are lined with abnormal, irregular endothelial cells displaying a great variability in wall thickness. These channels may be surrounded by hemorrhage and communicate through serosa, submucosa to mucosa, and even open into the bowel lumen proper. Cholesterol crystals may be found "snared" in these lesions. It seems unlikely that cholesterol crystals would be filtered by these tortuous vessels especially in the presence of active bleeding constantly "washing out" these vessels. Thus, the exact pathophysiologic development of these lesions remains obscure, but their association with gastrointestinal bleeding is well documented in the elderly, atherosclerotic patient with aortic stenosis.

Fig. 4B. Angiographic visualization of ectasia of the cecum: Late arterial phase demonstrating early visualization of dilated draining veins arising from vascular spaces (arrow).

The surgical management of this disorder is mostly one of securing a diagnosis with a defined site of bleeding. Extirpation of the involved segment of bowel results in resolution of bleeding. A right colectomy is rapidly performed and consideration need not be given to left sided diverticuli unless doubt as to the primary source of bleeding exists.

Summary

A case of angiodysplasia of the colon in the presence of extensive diverticulosis is presented with a discussion of the radiological diagnosis and pathological findings.

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The Ultimate Audit

Case Presentations

JOHN F. MURTAUGH, M.D., F.A.C.S.* and JOHN W. PETERSON, M.D.**

The Calais Regional Hospital is a 75-bed institution located in the northeast portion of Maine serving the rural population of eastern Washington County. On September 18, 1977, two emergency aneurysmectomies were carried out for abdominal aortic aneurysms. Both patients arrived one hour apart. Both patients survived. Their case reports and sequential events are as follows.

Case Reports

CASE 1: A 66-year-old male was admitted to the Calais Regional Hospital at 12:30 P.M. on September 18, 1977. He was brought to the hospital by one of the authors who was called to see the patient at his farm house. The patient complained of severe pain in the right side of his abdomen. This pain extended down his right anterior thigh and right testicle. This was accompanied by severe lumbar pain. A right iliac bruit was noted. This patient was known to have an abdominal aortic aneurysm approximately 6cm in diameter. A diagnosis of a rapidly expanding aneurysm was made and rupture could not be ruled out. Hct. 43, Hgb. 14.3, Urinalysis negative, BP 168/90. He was taken to the operating room at 2:00 P.M. An expanding abdominal aortic aneurysm was excised and a Dacron Y bypass graft was inserted. He received four units of blood during the procedure. Operating time was 3 and one-half hours. Postoperatively he received two units of blood. His postoperative course was uneventful except for a day of hyponatremia which was easily corrected. He was discharged on October 2, 1977. The patient is well and back working his farm.

CASE 2: A 73-year-old male was brought to the emergency room of the Calais Regional Hospital at 1:30 P.M. on September 18, 1977 just as Case 1 was entering the operating room. He complained of lower abdominal pain, left flank pain which radiated into his left testicle. Patient was well until the day of admission when he began to experience his pain. He had just driven a long way from Connecticut with his son to their camp in eastern Washington County. The patient was known to have been treated for hypertension in the past. On physical examination his BP was 148/88. His abdomen was soft with tenderness in the left lateral aspect and a left epigastric tender abdominal aortic pulsation was noted. A diagnosis of a ruptured abdominal aortic aneurysm was made. An AP and Lateral lumbar spine and an IVP were immediately obtained. The IVP findings were consistent with an aneurysm with ill-defined soft tissue densities in the retroperitoneal space on the left, displacing the left kidney and left ureter. The patient was typed and cross matched and prepared for surgery. He was taken to the operating room at 8:00 P.M. and a ruptured abdominal aortic aneurysm was found. This was resected and a Dacron Y graft inserted. The patient tolerated the procedure well and progressed satisfactorily immediately postoperatively. On his second postoperative day he developed diarrhea and cultures of the stools grew staph aureus. He also developed multiple premature ventricular beats. These were controlled with Lidocaine and Quinidine. He was placed on Cephalosporin for his staph enterocolitis. He responded to these treatment modalities but five days postoperatively he developed severe rectal bleeding. A nasogastric tube was inserted and confirmed upper GI bleeding. In spite of medical therapy, he continued to bleed and a upper GI series was obtained revealing a filling defect in the proximal stomach. He was returned to the operating room on his sixth day postaneurysm resection. This time he was found to have a large proximal gastric ulcer actively bleeding. The bleeder was ligated. Several small mucosal erosions were also found. A vagotomy and gastrojejunostomy was carried out. It was felt that due to the patient's precarious condition a resection should not be carried out at this time. A gastrostomy and a feeding jejunostomy were also performed. Once again he tolerated the surgery well. Postoperatively he was started on hyperalimentation and slowly and eventually was started on oral feedings. He was doing very well four weeks after admission and was getting ready for discharge when he suddenly developed right flank pain, shaking, chills and a WBC of 51,800. He was treated with Solu-Medrol®, Gentamycin, and Cephalexin. His blood cultures grew out E. Coli sensitive to Chloromycetin® and Gentamycin. He responded well to this therapy and became afebrile and asymptomatic. It was felt that he should have a liver, lung and perhaps a Gallium scan so five weeks after admission the patient was transferred to the Eastern Maine Medical Center. His scans were all negative. He was discharged from that institution to home. The patient is now back in Connecticut asymptomatic and doing very well.

Discussion

The resection of abdominal aortic aneurysm with insertion of synthetic grafts is a common operative procedure in major medical centers. It still remains a surgical procedure of magnitude with a relatively high mortality rate for those aneurysms that have ruptured or are rapidly expanding and massive blood transfusions are required.[1] The chance of two acutely symptomatic aneurysms arriving at an outlying rural hospital within one hour of each other seemed most unlikely. The fact that both patients indeed survived and have been discharged seemed to us worth reporting. When you consider that Case 2 survived the following, a ruptured abdominal aortic aneurysm, ventricular arrhythmias, staph entero-colitis, a bleeding gastric ulcer requiring gastric surgery, a week of hyperalimentation and an E. Coli septicemia, we felt that these cases are a tribute to the team approach developing in many rural hospitals.

We would also like to point out that although the family practitioner will always remain the backbone of rural medicine, the rural surgeon plays an important role in the scheme of things. A recent article in the November 1977 issue of this Journal[2] described the role of the internist in rural medicine. We present these two cases as an aid in delineating the capabilities of most well trained rural surgeons.

Summary

Two case reports of abdominal aortic aneurysms

Continued on Page 128

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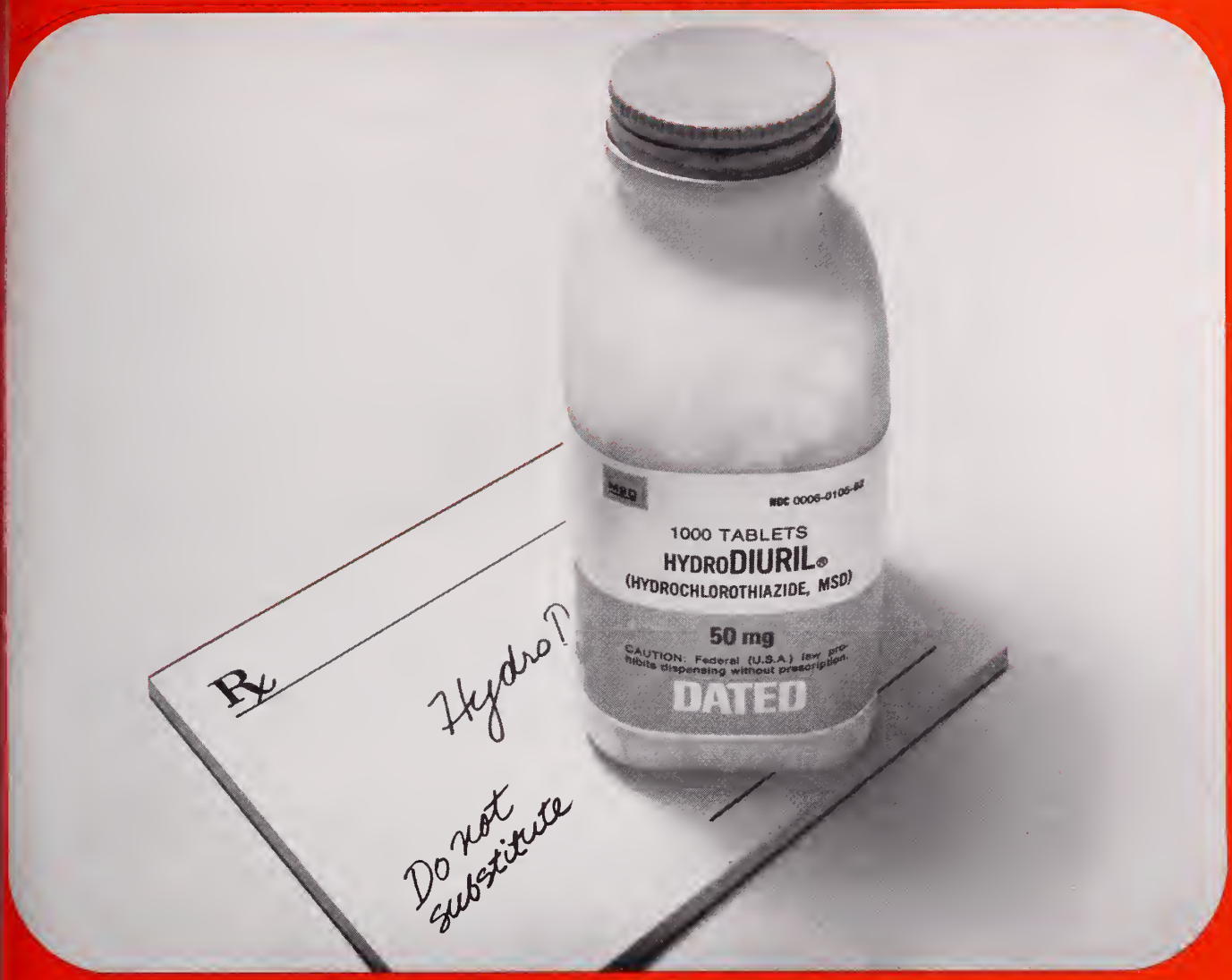
Contraindications: Anuria; hypersensitivity to this or other sulfonamide-derived drugs.
Warnings: Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects may develop in patients with impaired renal function. Use with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma. May add to or potentiate action of other antihypertensive drugs; potentiation occurs with ganglionic or peripheral adrenergic blocking drugs. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possibility of exacerbation or activation of systemic lupus erythematosus has been reported. Lithium generally should not be given with diuretics because they reduce its renal clearance and add a high risk of lithium toxicity. Read circulars for lithium preparations before use of such concomitant therapy. *Use in Pregnancy:* Thiazides cross placental barrier and appear in cord blood; in pregnancy, weigh anticipated benefit against possible hazards to fetus, including fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions that have occurred in adults. *Nursing Mothers:* Thiazides appear in breast milk; if use of drug is deemed essential, patient should stop nursing.
Precautions: Perform periodic determination of serum electrolytes to detect possible electrolyte imbalance. Observe all patients for clinical signs of fluid or electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting. Hypokalemia may develop, especially with brisk diuresis, in severe cirrhosis, with concomitant corticosteroid or ACTH therapy, or with inadequate oral electrolyte intake. Hypokalemia can sensitize or exaggerate response of heart to toxic effects of digitalis (e.g., increased ventricular irritability). Hypokalemia may be avoided or treated by use of potassium supplements, such as foods with a high potassium content. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt except in rare instances when the hyponatremia is life threatening. In actual salt depletion, appropriate replacement is the therapy of choice.
Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged; latent diabetes mellitus may become manifest. Thiazides may increase responsiveness to tubocurarine. Antihypertensive effects of the drug may be enhanced in postsympathectomy patients. May decrease arterial responsiveness to norepinephrine; this diminution is not sufficient to preclude effectiveness of the pressor agent for therapeutic use. If progressive renal im-

for experience—



or ours.

pairment becomes evident, consider withholding or discontinuing diuretic therapy. Thiazides may decrease serum PBI levels without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. Pathologic changes in the parathyroid gland with hypercalcemia and hypophosphatemia have been observed in a few patients on prolonged therapy; thiazides should be discontinued before testing for parathyroid function.

Adverse Reactions: *Gastrointestinal System*—Anorexia; gastric irritation; nausea; vomiting; cramping; diarrhea; constipation; jaundice (intrahepatic cholestatic jaundice); pancreatitis; sialadenitis.
Central Nervous System—Dizziness; vertigo; paresthesias; headache; xanthopsia.
Hematologic—Leukopenia; agranulocytosis; thrombocytopenia; aplastic anemia.
Cardiovascular—Orthostatic hypotension (may be aggravated by alcohol, barbiturates, or narcotics).
Hypersensitivity—Purpura; photosensitivity; rash; urticaria; necrotizing angiitis (vasculitis) (cutaneous vasculitis); fever; respiratory distress including pneumonitis; anaphylactic reactions.
Other—Hyperglycemia; glycosuria; hyperuricemia; muscle spasm; weakness; restlessness; transient blurred vision.
Whenever adverse reactions are moderate or severe, thiazide dosage should be reduced or therapy withdrawn.

Note: When used with other antihypertensive drugs, careful observations for changes in blood pressure must be made, especially during initial therapy. Dosage of other antihypertensive agents must be reduced by at least 50 percent as soon as this drug is added to the regimen. As blood pressure falls under the potentiating effect of this agent, further reduction in dosage, or even discontinuation, of other antihypertensive drugs may be necessary.

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Juvenile Manic-Depressive Illness Successfully Treated With Lithium Carbonate*

GEORGE MCNEIL, M.D., ALAN ELKINS, M.D. and HERBERT GOLDINGS, M.D.

In view of the success in treating manic-depressive illness with lithium carbonate, there has been a thrust to broaden the diagnostic category.[1,2] Patients previously seen as schizophrenic treatment failures may now be reviewed, in the light of atypical manic-depressive illness, for a trial on lithium carbonate. In like manner, although the disease is felt traditionally to be one of adults, there is a beginning awareness of manic-depressive illness in the pediatric age group.[4,5,6,7] We would like to report one such case, successfully managed with lithium carbonate.

Case Presentation

A sixteen-year-old high school student was admitted to the hospital after her parents noted a bizarre behavior of five to six days' duration. They reported a marked increase in motor activity during this time; and they finally had to resort to physical restraint, lest the patient wander into the street. They also noted outbursts of ill temper. There were no apparent precipitants to this behavior.

Family history revealed her to be the second of six siblings, ranging in age from seventeen to ten. There was no family history of major affective disorder. Mother did report an episode of mild depression treated with short term psychotherapy. Mother also reported a brother with color blindness.

Early growth and development were unremarkable, except for difficulty with multiple food and respiratory allergies. The early school years were seen as quite successful. The family noted a marked change, however, when the patient was age thirteen. She seemed then to become more outgoing, but at the same time she began to have periods of depression. These seemed to be unrelated to life events, and the first such episode was marked by a suicide gesture by pill overdose.

She was seen briefly in psychotherapy, but continued to have periodic depressions, lasting one to two weeks, during which time she often would not get out of bed. She frequently moved directly from these to a state of "high." Over the several months preceding admission these "highs" became more bizarre; and her friends began describing her as "high without drugs."

Mental status exam on admission revealed a neatly dressed girl who spoke with flamboyant, descriptive hand gestures, at times substituting gestures for speech. Affect was light, and she appeared indifferent to recent problems at home. Stream of thought was markedly tangential. In addition, she described perception that her parents behaved as strangers and that she was being ostracized from the family. She wondered whether she might be "possessed." There were no hallucinations. She was not suicidal or homicidal. Tests of sensorium were unremarkable with the exception of digit recall. Here she spewed back numbers in what seemed to be purposeful disarray. Proverb interpretation was extremely concrete. Insight was impaired to the point where she felt the illness to be in her family and not herself.

Seen initially as representing a schizophrenic disorder, she was treated with gradually increasing doses of major tranquilizers. Despite adequate trials of first, chlorpromazine, then perphenazine, then haloperidol and despite the presence of a consistent and highly structured ward milieu, she followed an erratic course. Her bizarre and hyperactive behavior resolved only to give way to a period of profound withdrawal and anergy. This, in turn, was followed by recrudescence of wild behavior.

At this juncture, lithium carbonate was begun. At low doses of drug, with serum lithium levels 0.7 mEQ/L or below, she had continuation of labile affect and regressed behavior. But with increase of lithium carbonate to 1500mg a day, pushing the blood level to 1.0 mEQ/L, lability and disorganization were modulated.

After one month of lithium her behavior was seen as normal. At this time, she began to be able to deal with age-appropriate issues in psychotherapy and to be able to start intergrating the impact of her illness on her life.

In the seven months since discharge from hospital she has been continued on lithium and has had absence of major mood swings. She is functioning satisfactorily in school and social settings.

Discussion

Recognition of manic depressive illness in the pediatric age group remains uncommon.

Annell[8] published a series of five children, ages eight to fifteen, successfully treated with lithium carbonate. She also reviewed the literature (dominated entirely by European workers) of juvenile manic-depressive illness. More recently, Berg, *et al*[9] described a fourteen-year-old girl with manic-depressive psychosis responsive to lithium carbonate and a fifteen-year-old mentally retarded girl with typical diphasic mood swings.

The infrequent diagnosis of childhood or juvenile manic-depressive illness is of interest. Speil[11] points out that childhood depression is rarely as evident as the adult variety. Sad affect and verbal lamentations tend not to be seen but are replaced by psychosomatic illness or changes in motor activity. Similarly, mania might readily be confused with hyperactivity in this age group. Hava[12] has recently proposed that at least some children now diagnosed as hyperactive or minimally brain damaged may be lithium responders.

In 1960, Anthony and Scott[13] offered ten criteria for this diagnosis:

1. Evidence of abnormal psychiatric state at some time during the illness which approximates the classical clinical description.
2. Evidence of a "positive" family history suggesting manic-depressive diathesis.
3. Evidence of an early tendency toward a manic-depressive type of reaction as manifested in a) Cyclothymic tendency with gradually increasing amplitude or length of the oscillation, and b) Delerious manic or

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depressive outbursts occurring during pyrexial illness.

4. Evidence of recurrent or periodic illness with at least two of these episodes. There should be diagnostic agreement by different clinical judges on the nature of any one episode and by different clinical judges on the identity of different episodes.
5. Evidence of a diphasic illness showing swings of pathological dimensions from state of elation to state of depression and vice versa.
6. Evidence of an endogeneous illness indicating that the phase of the illness shows minimal reference to environmental events.
7. Evidence of illness as indicated by the need for inpatient treatment, heavy sedation and ECT.
8. Evidence of an abnormal underlying personality of an extroverted type demonstrated by objective test procedures.
9. An absence of features of schizophrenia or organic states.
10. Evidence of current, not retrospective assessment.[14]

Our patient fulfills nine of these criteria, failing only to have a clearly positive family history.

Summary

There is a growing body of literature to attest to increasing awareness of manic-depressive illness in childhood and adolescence. We briefly review this and report the case of a fifteen-year-old girl with manic-depressive illness of at least two years' duration, who has been successfully treated with lithium carbonate.

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CONTROL OR CONFUSION?: Hospital Employee Tuberculosis Surveillance

Continued from Page 108

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Maine Medical Center

The Physician and Medical Care Costs

A Summary of the Phase-1 Report of the Medical Costs Study Committee of Maine Medical Center

January 24, 1978

This ad hoc committee was established one year ago in recognition of widely-expressed concern about the rapidly rising expenses of medical care and because of our belief that physicians must, and can, do something about their share in this large and complex problem. It is clear that the burdens of paying for health care result from multiple factors, most of which are beyond the direct control of physicians and outside the scope of this committee's studies. Commonly cited are such major factors as: inflation; a rising proportion of elderly people; increasing use of medical care by a more affluent, more insured and more urbanized population; development of new more costly diagnostic and therapeutic tools; and mounting malpractice suits and premiums. In addition and to an unmeasurable extent are current life styles and environmental pressures tending to produce or enhance a wide variety of illnesses (e.g., cancer, accidental injuries, cardiovascular and pulmonary disorders, and alcoholism and other drug abuses). Nonetheless, the physician, as the principal gate-keeper to medical care, is one of the key figures in cost control.

In the daily press and in medical journals, skeptics express doubt that physicians can be influenced to do much in cost-saving; they are described as often resistant to change, reluctant to alter long-established habits. If this be true, the most effective point of leverage may be in medical student and resident training.

In monthly meetings we have scanned suggestions about cost-saving collected from varied sources. We have discussed in detail a few of the most pertinent, finding it difficult to sift out what is feasible and worth emphasis, and attempting to focus on those costs which are generated by the physician at MMC.

One separate item, not directly a physician responsibility, was reviewed and then passed on to the Dietary Advisory Committee. We suggested closer supervision of the general menu offered inpatients, aimed at curbing over-selection by patients and wasting of food. David Lieberman, Assistant Administrator, has recently reported informally that some progress, of uncertain degree, has been made.

Conclusions

At this point we have reached the following general conclusions:

1. It should be possible to control some of the excessive costs of health care for which physicians are responsible without compromising its quality. In some instances, ordering less and doing less to a patient may yield better care for him. And, in a broader view, if and when firm limits are set on total medical costs, money ill-spent will thereby be unavailable for quality care elsewhere.

2. Cost control must come mainly from those who order tests and procedures, rather than from the providers (e.g., the laboratories, pharmacy and medical supply department).

3. A major goal must be to enhance cost-consciousness in physicians, using several kinds of education at various levels and by repeated efforts. In some instances of excessive or inappropriate ordering, specific re-education may produce only minor savings, yet any effort is worth making which induces the physician to examine his own behavior and to become more cost-aware.

4. In discussions of medical costs two particular factors are often cited as major contributors: a) an excess of diagnostic tests in teaching hospitals, ordered by inexperienced residents striving too vigorously or aimlessly to be thorough, and b) a similar excess of tests in the practice of 'defensive' medicine, in response to the rising tide of malpractice suits. Both of these forces may be at work, but it is impossible to measure the degree of either. In the first instance, for example, a relative increase in tests does not per se prove poor judgment. More testing of some patients may denote a keener awareness of the dimensions of the clinical problems and of a legitimate need for multiple and special investigations. The teaching hospital, moreover, tends to attract a disproportionately large number of patients with obscure or complex illnesses requiring intensive and sometimes extended studies.

Recommendations

1. Closer supervision in teaching hospitals by senior residents and attending physicians of the ordering habits of medical students and housestaff on all clinical services; they need to curb the overuse of tests and procedures, including the custom of "running" orders for certain daily tests, and to eliminate the use of outmoded methods of study and treatment. All this obviously requires experience and sound judgment.

2. Better education of physicians concerning the prices of common tests and procedures by such devices as: a sample audit of a patient's mounting hospital bill by his student physician; by discussion of a typical hospital bill at a monthly staff meeting; by a panel discussion at a staff or departmental meeting of common patterns of over-ordering; and by displays, as in the Doctor's Lounge, of the costs of selected items.

3. Notification of the staff that on request through the Controller's Office a copy can be obtained by any physician of his patient's itemized hospital bill, for the physician's review and enlightenment.

4. Periodic presentations at staff or departmental meetings of results of cost-benefit studies now underway in various medical centers, and of developing strategies in clinical decision-making.

5. Urging of the Administration and the Department of Nursing to include cost-saving questions on the agenda of their standing committees. We have suggestions to offer.

Additional Comments

In retrospect, progress by this committee has been halting, reflecting largely the complex nature of cost factors in medicine, but also the reluctance of some to recommend actions which would impinge on the practice of colleagues. Accordingly, the recommendations above call mainly for better education to modify physician behavior and stress persuasive rather than coercive methods. The suggestions tend to blandness, with little or no bite.

But many tough questions remain. Some have been raised by insurance companies or governmental agencies and soon rather than late should be reviewed by this or some other committee of Maine Medical Center (or a medical society at the County or State level). Whatever recommendations result can, and in some instances should, rely on something more than earnest persuasion. Possible actions, each needing much debate, include:

1. Closer review by the Medical Audit Committees of the ordering of tests and procedures to identify patterns of overuse of certain items or by certain physicians;

2. Limitation on the ordering of certain very costly tests to attending or consultant physicians;

3. Mandatory 'second opinions' by another surgeon or consultant before certain elective surgical procedures;

4. Active participation by clinical laboratories in detection of overuse or misuse of certain tests;

5. Evaluation of risks of overuse of costly diagnostic tests by physicians owning and profiting from the equipment;

6. Reorganization of hospital schedules to offer all services on a 7-day per week basis;

7. Evaluation of cost-effectiveness of various community screening programs and of the 'annual physical examination' in the physicians' office.

Scientific advances which yield new costly methods for diagnosis or treatment already have raised special problems. At some point "health care providers" may have to set limits on the use of some of these tools, conceding that society cannot afford everything that is available for the study and care of every sick patient everywhere. Physicians, in particular, will undoubtedly face hard choices in setting priorities for purchase and use of new equipment, whether in office or hospital, and may have to prefer what will offer the greatest good to the largest number of patients. They will need to practice what has been succinctly termed "technologic restraint."

Deliberately omitted from our consideration are the important issues attached to the high cost of dying, especially when this involves inappropriate use of complex life-support techniques. This topic touches on major clinical, ethical, philosophic and legal questions which are well beyond the reasonable range of this committee at this time.

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Annual Meeting Dates For Your 1978 Calendar . . .

Maine Medical Association, June 10-13
Treadway-Samoset, Rockport, Maine

American Medical Association, June 17-22
St. Louis

A Rural Primary Care Student Preceptorship

DANIEL K. ONION, M.D., M.P.H.*

ABSTRACT

A medical and dental student preceptorship sponsored by a rural group practice successfully recruited students, provided professionally stimulating teaching opportunities for group members, and helped students understand problems in rural health care. The preceptorship has also enhanced the group's recruitment capabilities in two ways, by the direct recruitment of former students and by making positions with the group more attractive to well-trained health professionals. Since the expiration of federally funded startup period, support from the group practice, state agencies and several medical schools has assured the preceptorship's continuing existence.

INTRODUCTION

Most medical and other health professions student preceptorships in this country derive their origin and ongoing primary support either from the professional schools themselves or student groups. Preceptor initiated programs are relatively rare. However, our rural group practice of medicine and dentistry has organized, sponsored, and filled a formal student preceptorship program since 1975. Developed primarily as a response to the group's perceived national need for rural preceptorships, the program appears to also be a good recruiting vehicle. A questionnaire revealed that student attitudes toward various aspects of rural practice changed during the preceptorship. Varieties of selection criteria, course length, and course content were tried; the apparently best and worst of these are discussed.

BACKGROUND

Rural Health Associates (RHA) is a community-based non-profit health services corporation in West Central Maine formed in 1969 through the joint efforts of a group of local physicians and the local Community Action Program. A multi-specialty group practice of medicine, dentistry, optometry, and pharmacy, which now includes twenty providers (twelve M.D.'s), grew from this effort. The organization concomitantly developed a prepaid health plan (Health Maintenance Organization), three satellite offices, and a central facility near the local community hospital, an extensive outreach/social worker system, a multiple ongoing school/community health education and screening projects. Interactive television communication between the satellites and the central facility were developed. Several physician and dentist extenders improve provider efficiency.

As the group evolved, health professions' students requested and did one or two month preceptorships with group members. Most students wanted the experience primarily to see and feel what real practice in a rural, non-university setting was like. For the first four years of RHA's existence, no prerequisites were required of students besides their interest and their own funding. Their curriculum was an individual one arranged by their preceptor.

In 1974, RHA, as an organization, entered a second, more formal phase of student training and decided to sponsor an ongoing preceptorship for medical and dental students.

PROGRAM OBJECTIVES

RHA developed the preceptorship with three primary goals. First, we saw it as a partial remedy for a dearth of good non-university based rural preceptorships. Our preceptors felt that their own adaptation to rural practice had in many instances been facilitated by a similar experience. We wanted the student to understand the social milieu well enough so that he/she someday might attempt rural practice with more open eyes, less romance, and more understanding of the political and social issues. Secondly, medical student teaching is perceived by our professional staff to be an important part of their own continuing education. We also found that the presence of the student program made the group more attractive to new physicians interested in joining the group. Finally, we hoped that, given such an experience, some of the students might return to West Central Maine and RHA to practice.

PROGRAM DESIGN

The preceptorship was defined as a two-month experience in rural primary care, dental or medical. We chose two months because our past experiences indicated that students took nearly a month to become oriented to our health care system. Both students and preceptors felt that much more clinical and community medicine was learned in the second month. Longer preceptorships were difficult for students at most schools.

With a few exceptions, we excluded students who had not had at least six months of their medical school clinical rotations. Students with lesser experience impaired our practitioner's ability to see a normal volume of patients, a paramount concern in a rural area with a doctor to patient ratio of 1:1500 or 2000.

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This project was supported in part by contract number NO1-MB-44191 from the Office of Interdisciplinary Programs, Bureau of Health Manpower, Health Resources Administration, Department of Health, Education & Welfare.

A preceptorship application form on which students described their reasons for electing this preceptorship and their goals served to screen out students whose goals we could not meet.

Each student was matched with a primary care preceptor with whom the student spent eighty percent of his/her professional time during the two months. During this clinical preceptorship time, the student saw and was the primary health care provider for one-third to one-half of his/her preceptor's normal patient load in the hospital, the emergency room and the offices. Most patients were seen, at least briefly, by the preceptor also during each encounter. But initial evaluation, problem formulation, and diagnosis and therapeutic planning were done first by the student; and then presented by the student to the preceptor. The students shared their preceptor's call schedule, and in their off time were encouraged to enjoy rural social and sports activities which the area offers like agricultural fairs, skiing, fishing, etc.

Twenty percent of the student's time was devoted to studying issues in rural medical sociology. The students conducted weekly two-hour seminars in which they debated non-clinical topics relevant to rural health care. We chose the debate format because it appeared to encourage freer student participation and discouraged premature conclusions. At the end of the eight weeks, the students were required to write a paper on a medical sociologic issue, discussing it in local and national terms.

The seminar segment of the preceptorship was instituted because we found that students tended to discuss only clinical medicine/dentistry with their preceptors. The RHA staff felt that further preparation in the sociologic dynamics of rural health care was important to the students' understanding of rural health problems.

The HEW Office of Interdisciplinary Programs of the Bureau of Health Manpower, agreed to help finance the ongoing preceptorship especially in order to expose students to a rural Health Maintenance Organization (prepaid health plan). Students received a transportation allowance to and from the preceptorship site and home, and during the preceptorship, an allowance toward board. RHA rented apartments for student use. During the first two experimental years of the project, we required an on-site interview before accepting a student. The student costs for this interview were reimbursed.

Results and Discussion

The Two-Year Experience

During the first six months of the project, we publicized the preceptorship to all northeastern medical and dental schools: many included it in their elective curriculum books. All schools gave students academic credit for the preceptorship, in many cases allowing it to be substituted for university primary care rotations. We found that, unlike medical schools, most dental schools had little elective time in which their students might participate in such a preceptorship. Tufts Dental School, however, did have such a curriculum, and so eight dental students from Tufts participated.

Table 1

Seminar Topics

1. Resolved that there should be central control of type and distribution of health care personnel.
2. Resolved that all health care training should take place in universities.
3. Resolved that all health practitioners should practice in a group.
4. Resolved that all records should be kept in a POMR system.
5. Resolved that all health practitioners should be retested every five years.
6. Resolved that all health care should be provided by a prepaid HMO model.
7. Resolved that all health practitioners should be salaried.
8. Resolved that P.A.'s and hygienists are second class health care.
9. Resolved that health education is futile.
10. Resolved that preventive medicine is cost ineffective.
11. Resolved that chiropractors should be prevented from practicing.
12. Resolved that every community should be allowed to plan its own health facilities without governmental interference.
13. Resolved that national health insurance is the answer.
14. Resolved that we need more doctors/dentists.
15. Resolved that peer review is the best public hope for assuring quality care.
16. Resolved that computers should be used more extensively in medical care.
17. Resolved that rural health problems are basically those of any group in this country and require no special approach.
18. Resolved that family practice is not a viable specialty.
19. Resolved that women should not be doctors/dentists.
20. Resolved that health services should be able to advertise.
21. Resolved that physicians should be required to deliver emergency medical care.
22. Resolved that the fear of malpractice interferes with the provision of quality health care.

Forty-two medical students applied; twenty participated in the preceptorship. Of the other twenty, we rejected only two. The rest could not be accepted because the rotations they requested had already been filled.

Their numbers, by school of origin:

Ohio State	5
Yale	3
Case Western Reserve University	3
University of Pennsylvania	3
University of Missouri	2
University of Connecticut	1
Tufts School of Medicine	1
Boston University	1
New Jersey College of Medicine	1

Each rotation of students chose the debate issues from the previously established lists of topics and usually suggested and debated new topics as well. The projects' xerox library of relevant articles for each topic expanded accordingly and was updated by each group of students. We found that the best debates were elicited by a very polarized, controversial statement, hence the inflammatory debate titles (see Table 1).

Of the papers each student wrote during the preceptorship, four have been submitted to various journals for publication and two have been published.

What RHA Learned

The preceptorship length, primary care orientation, clinical and seminar content and prerequisites proved to be successful and popular with preceptors and students. Occasional attempts to shorten the experience to one month resulted in mutually less satisfactory preceptorships. We found that preacceptance interviews were difficult to arrange with both students and preceptors; these interviews resulted in reversal of an acceptance decision less than ten percent of the time and were therefore dropped. Payment for transportation to and from the area proved to be unexpected and relatively unimportant to students and was also eliminated. Some stipend for temporary housing and board was, however, crucial to student participation, surprisingly even more so than medical school approval of the preceptorship for credit.

Malpractice costs did not change with the preceptorship. Physician/dentist productivity, as measured by patient volume and generation, did not change, either up or down, during preceptorship. Most providers estimated that their average work week was extended three or four hours during a preceptorship; but they found this acceptable when preceptorship periods were rotated among providers. Practice space was a problem; but we found that providers could manage if each primary preceptor had three available examination rooms when precepting a student.

During the course of the project, nursing, physician assistant and health administration students requested preceptorships and were successfully incorporated into the curriculum with appropriate preceptors in their fields.

At the conclusion of the HEW funded project, RHA was resolved to continue a multi-disciplinary student preceptorship and continued to do so with varying funding sources. The organization's goals of a professionally satisfying ongoing teaching program in rural health care had been realized; the subsequent joining of the group practice by a dentist who had participated in the dental student preceptorship also suggested that secondary, long-term recruitment goals might also be realized.

Student Attitudes

Student attitudes about rural practice and living, as well as various possible solutions to rural health problems were surveyed at the beginning and end of the preceptorship.

Student attitudes were positively changed in two areas. Although skeptical on arriving, they came to view a prepaid or Health Maintenance Organization as a viable approach to rural health care. Their con-

Continued on Page 128

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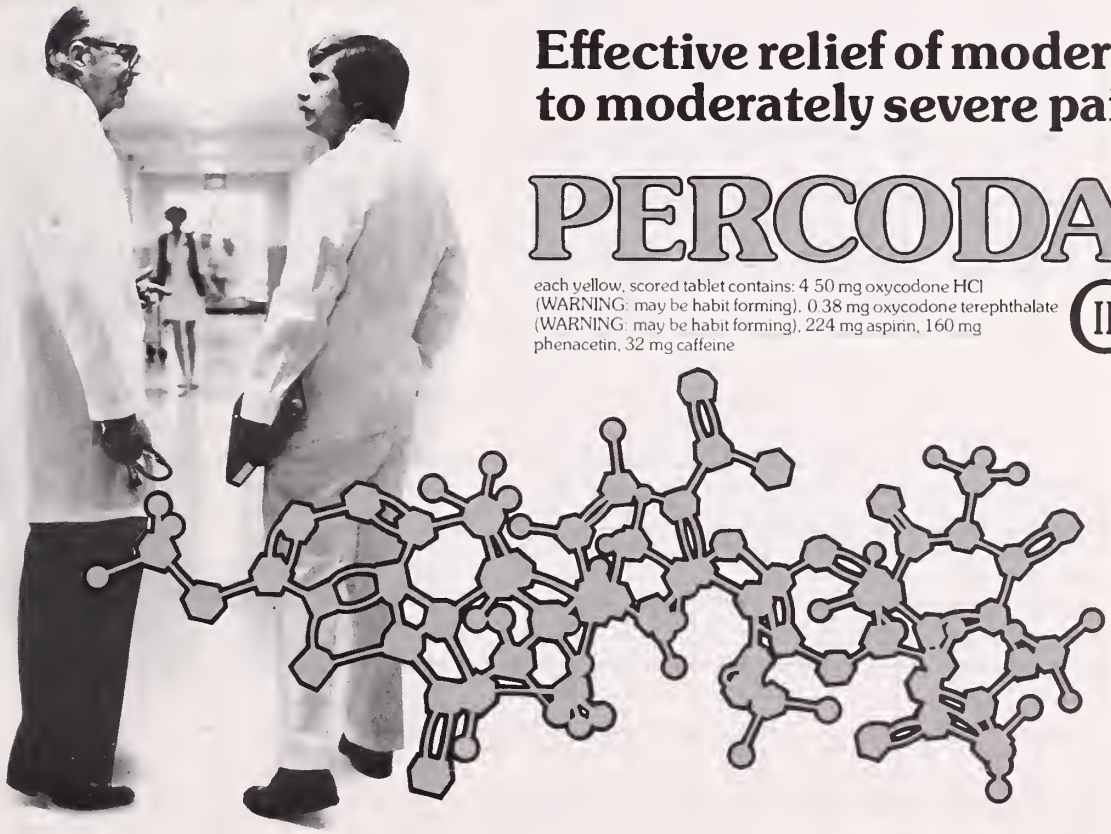

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cerns about the impossibility of practicing quality medicine/dentistry in a rural area were dispelled.

Students' initial confidence in many techniques for alleviating health problems remained unshaken; specifically, physician assistants/hygienists/nurse practitioners, transportation networks, outreach/social workers, interactive television, computerization, and group practice.

Students arrived with high expectations for the effects of health education on a population's health. Surprisingly they left with much deflated hopes for health education.

Conclusion

A rural health care organization has initiated and sponsored an ongoing student preceptorship. Debate format seminars have helped the student expand and generalize from the preceptorship experience itself to more global sociologic issues. The preceptorship proved to satisfy the group practice's major goals of participating in medical/dental student clinical and sociologic teaching. After the initial two-year HEW funding, continued support has been successfully found from multiple sources. The preceptorship has achieved a popularity with northeastern medical students to a point that RHA can accept only about one-half the students who now apply.

Acknowledgments

The author appreciates critiques of earlier manuscript drafts by Naomi Quenk, Ph.D., and Ronald B. Merrill. Peter Doran, Ph.D., helped develop, administer, and evaluate the student attitudinal questionnaire.

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THE ULTIMATE AUDIT: Case Presentations — *Continued from Page 117*

requiring emergency surgery within one hour of each other at an outlying rural hospital are described. The role of rural surgeons has been stressed. Whether one chooses to practice in an urban or rural setting, and in these days of multiple audits, the ultimate audit will always be the patient, his pathology, and his timing. We as rural surgeons must be prepared for this challenge.

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Extensor Tenosynovitis of the Hand From Cold Exposure

JAMES GEORGITIS, M.D.*

Frostbite is usually diagnosed on the basis of history and of skin manifestations ranging from erythema to necrosis. Because of the imperfect thermal conduction of human tissue, areas of injury may not correspond to what is felt to be the area of exposure and attention is usually directed to the skin with little appreciation of involvement of deeper structures. The full extent of injury may be unappreciated for an extended period. Three cases with tenosynovitis of the extensor tendons of the hand without dermal necrosis are presented as examples of a more subtle presentation of frostbite.

CASE 1

A forty-one-year-old white male presented with a six day history of persistent pain in the left hand following cold exposure during fourteen hours of riding in an open-top jeep with ambient temperatures of 20° to 30° F (–6° to 0° C). His hand had been exposed to wind, but protected by a knitted insert and leather outer glove. There was no past history of trauma or inflammatory joint or tendon disease. Physical examination revealed marked erythema and edema of the dorsum of the hand extending to the dorsal flexor crease of the wrist. Crepitation and pain with movement were present over the extensor tendons of the index and ring fingers with slight crepitation over the extensor tendon to the middle finger. Serum uric acid, Antinuclear Antibody titer (ANA), LE-prep, rheumatoid factor, and cold agglutinin tests were all within normal limits. Treatment was initiated with five grains of aspirin orally every four hours, hot soaks for thirty minutes four times a day, and splinting in a position of function. After ten days of treatment, pain and crepitation were still present with slight edema over the dorsum of the hand. Infiltration of 15 mgm of hydrocortisone into the extensor tendon sheaths resulted in resolution of all signs of inflammation in forty-eight hours without pain and with return of a full range of motion.

CASE 2

A thirty-seven-year-old white male presented with pain in the left hand of recent onset, noted while grasping objects. He had been riding in an open-top jeep for ten hours with his hand protected by unlined leather gloves. Ambient temperature ranged from 20° to 30° F (–6° to 0° C). There was no past history of inflammatory tendon or joint disease or antecedent trauma. Physical exam revealed pitting edema of the dorsum of the hand extending to the flexor crease of the wrist, slight erythema and crepitation over the extensor tendons to the index, middle and ring fingers. Radiographs showed no evidence of old or recent trauma. Serum uric acid, ANA, LE-prep, rheumatoid factor, and cold agglutinins were all within normal limits. The patient was treated by immediate warm immersion of the hand, oral aspirin, and splinting in a position of function. In seventy-two hours, pain-free movement was present with complete resolution of edema and crepitation.

CASE 3

A thirty-six-year-old white male presented with a twenty-four hour history of acute onset of pain with movement of the fingers of the right hand. There was no previous history of trauma or inflammatory joint or tendon disease. The preceding history was of riding in an open-top jeep for sixteen hours with hands protected by knitted inserts and outer leather gloves. The temperature range at the time was from 5° to 30° (–25° to 0° C). Physical examination revealed swelling over the dorsum of the hand up to the flexor crease and crepitation over the course of the extensor tendon of the index and ring fingers. Treatment with warm immersion and oral aspirin resulted in resolution of the condition in forty-eight hours despite re-exposure to cold.

DISCUSSION

These cases represent an unrecognized form of cold injury, apparently overlooked in the past because the skin manifestations are not striking. All cases presented because of pain. Swelling and crepitation were not noted by the patients. The average temperature was not obviously severe but the wind-chill factor at an average jeep speed of thirty miles an hour resulted in –18° to –48° C temperatures.

The pathogenesis of extensor tenosynovitis of the hand appears to be similar to the pathogenesis of more severe degrees of cold injury. Hands are vulnerable to cold injury because of their surface area to volume ratio and frequent exposure.[1] Rapid shunting of warm arteriolar blood to the superficial venous network protects the hands during cold exposure but also rapidly releases heat to the environment. This physiological protective mechanism, when prolonged, sacrifices positive heat balance and leads to a drop in core body temperature. This results in reflexive vasoconstriction and discontinuation of the arteriolar-venous shunt. This reaction (Lewis-Hunter reaction) of vasodilitation followed by vasoconstriction explains why, even in the presence of thermal insulating clothing, cold injury will occur.[2] No surface body heat is available to warm the skin or thermo-insulating boundary. If further vasoconstriction continues, tissue perfusion decreases and resultant hypoxia ensues. Sensory nerve function ceases when ten degrees centigrade surface temperature is reached, removing the sensory warning of continued tissue injury.

The pathogenesis of tissue injury at the cellular level is multifactoral (Figure 1) with all factors not clearly delineated. Direct metabolic impairment due to cold and intracellular water crystallization are known to occur. Crystallization causes an increase in intracellular osmolarity. Differential suppression of enzyme systems, nuclear and mitochondrial plasma membrane changes follow "momentary" cold exposure.[1] With prolonged cold exposure serum (SGOT, LDH) enzyme elevations have been noted indicating loss of plasma membrane integrity. Denaturization of lipoprotein and formation of precipitation complexes have also been documented.[3]

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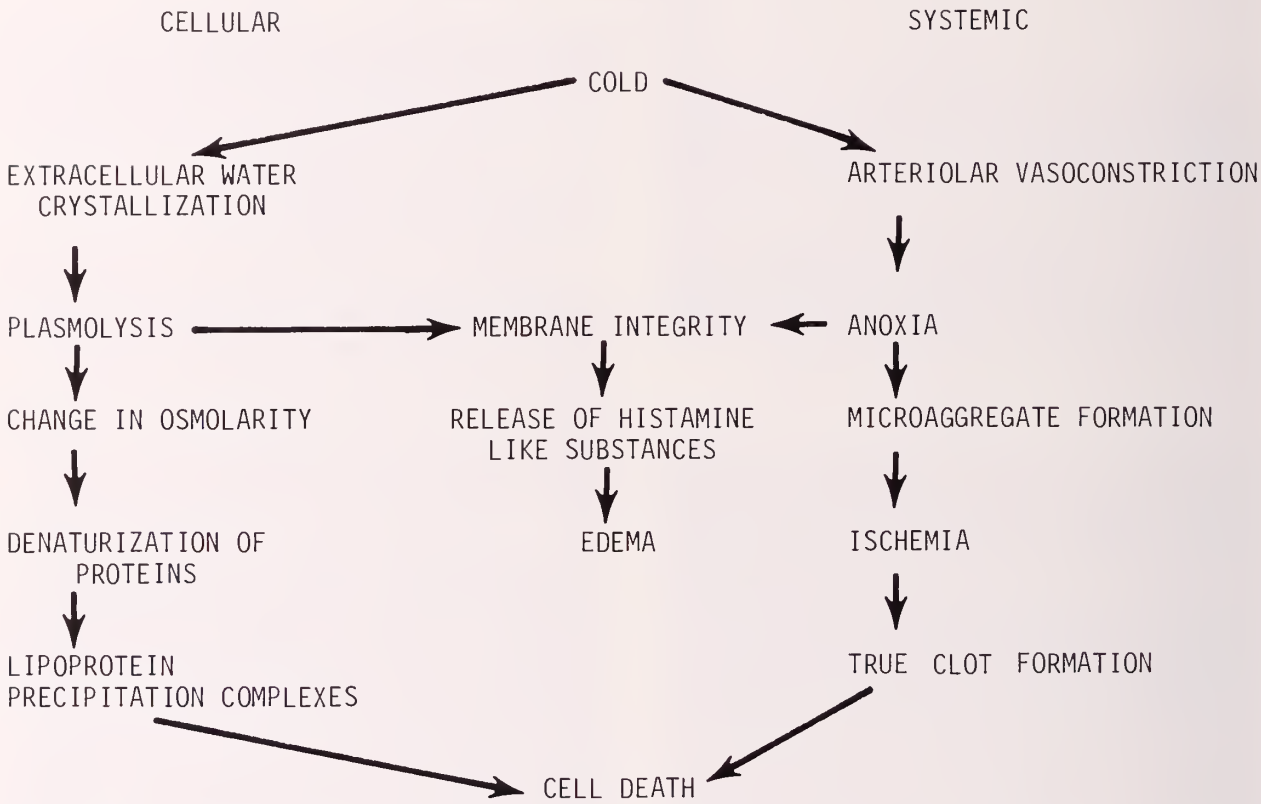
FIGURE 1

SCHEMATIC DIAGRAM OF SOME OF THE PHYSIOLOGICAL EVENTS OF COLD INJURY



Intracellular hyperosmolarity consequent to extracellular water crystallization produces plasmolysis with resultant cellular dehydration. This induces cellular death through enzymatic and protein denaturization and colloid formation.[4,5]

Vascular changes ensue from systemic and endothelial cellular changes. Vasoconstriction results in vascular stasis, cellular aggregation of blood elements and microthrombus formation. Microthrombus formation predisposes to true clot formation with its resultant occlusive tissue hypoxia.[5] Corpuscular clumping creates microcirculatory occlusion, thus jeopardizing the precarious viability of already cold-traumatized cells.

Certain prognostications can be made on the basis of weather at the time of injury and physical findings when the patient is first seen for treatment. Predominantly subfreezing temperature, high humidity, precipitation and wind with exposure for more than ten hours result in clinical frostbite. Large clear blebs, rapid return of sensation, rapid return of normothermia and good capillary filling are good prognostic indicators. Indications of greater injury with poorer prognosis are white, cold asensory skin without blebs and absence of edema. Cyanotic skin with hemorrhagic blebs and early mummification associated with constitutional signs of tissue necrosis herald extensive injury.

Treatment should be aimed at the reversal and modification of the physiological events wrought by cold. The goals are maximum preservation of tissue and function. Cardinal rules include conservative surgical management with careful observation over a period of time, realizing that the full extent of injury may not be readily apparent on initial evaluation. Treatment starts with removal of constrictive clothing, limited weight bearing and immediate immersion in heated water to reverse hypothermia. Submersion of the injured extremity in a bath between 40° and 42° C until the part becomes pink and sensation has returned is well established as the initial treatment.[6] Bedrest in a sterile environment, no smoking, and warm IV fluids follow initial immersion if systemic hypothermia is not present. When systemic hypothermia is present, aggressive treatment is directed at raising core temperature, protecting renal output, and reversing systemic hypokalemia. Intracellular migration of potassium may be severe enough to result in cardiac arrhythmias which may be responsive to beta adrenergic blockade. Relief of pain, observation for infection, placement of light nonconstrictive

dressings and elevation of the injured extremity follow initial treatment. Debridement of vesicles is contraindicated. Tetanus toxoid 0.5 cc intramuscular should be administered and antibiotics selected on the basis of appropriate clinical and laboratory signs of infection. As with burns, periodic wound cultures enable the physician to make a more accurate first drug choice to treat a rapidly developing infection. Whirlpool debridement and active physiotherapy are used to facilitate recovery.[7]

Controversial treatments include the application of pressure dressing to prevent edema formation, antihistamines and steroids to counter histamine-like substances which may be released causing edema and exciting an inflammatory reaction and intravenous heparin or low molecular weight Dextran® during the first thirty-six hours following insult. The use of systemic and local vasodilators combined with sympathectomy or the use of sympathectomy alone have been used to reverse the extent of vasospasm.[6,8,9,10] The efficacy of sympathectomy has not been established and it may actually increase tissue ischemia by inducting systemic hypotension following sympathectomy. Intravascular injection of reserpine has also been shown to reverse the vasoconstrictive effects of cold injury.[14]

Surgical debridement should be minimized until the full extent of injury is known. Early spontaneous eschar separation may expose good granulation surfaces, permit immediate skin grafting and physiotherapy. More precise indications for surgical intervention are the release of constricting superficial bands of hard circumferential eschar which cause distal ischemia.

Sequellae to cold injury reflect to a certain extent the degree of severity of the original injury. Common sequellae to first and second degree frostbite are hyperhidrosis, dull pain on re-exposure to cold, "cold" sensation and numbness. Depigmentation of the skin at the site of injury and abnormalities of nail growth may follow cold injury. Stiffness of joints, especially pronounced in cool weather, may be the most disabling sequela to cold injury.

Hyperhidrosis suggests a sympathetic nervous system disorder following frostbite. Appropriate sympathectomy can alleviate this condition if it becomes excessive. Skin blanching and pain may mimic Raynaud's phenomenon in the upper extremity. Late changes of depigmentation or erythrocyanosis result from primary damage to melanophores. Joint disease may become extensive with scar contracture and lytic bone lesions.

No sequellae other than an increased sensitivity to cold was noted by the three patients who presented with cold-induced tenosynovitis. One patient noted a return of "crackling and pain" on re-exposure to cold but the condition resolved spontaneously and no history of cold urticaria was found.

Summary

A previously unreported form of cold injury to the hands, consisting of sterile extensor tenosynovitis is described in these patients. Early reversal of symptoms and findings with warmth and aspirin followed treatment within twenty-four hours of injury in two patients. Local injections of hydrocortisone was used in one patient whose initial treatment was delayed six days.

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MEDICARE PREMIUMS/COMPANION PLAN RATES TO CHANGE

Medicare beneficiaries who voluntarily enroll in the program's supplemental medical insurance — Part B — that helps pay for physicians' bills and a variety of other medical expenses will pay 50 cents more every month beginning July 1, 1978, the Department of Health, Education and Welfare announced recently. The monthly premium will increase from $7.70 to $8.20.

On the same date, the premium for Part A — Hospital insurance — will rise from $54 to $63 for those elderly Americans who are not automatically eligible for Medicare but who voluntarily enroll in this part of the Medicare program.

At present there are only 21,000 such voluntary enrollees, since the majority of Medicare beneficiaries have their Part A premium paid for by their Social Security.

It was also announced last fall that effective January 1, 1978, the Medicare Part A deductible of $124 would increase to $144. Since 1973, this deductible has doubled — from $72 to $144 — a full 100 percent increase.

Since Blue Cross and Blue Shield of Maine's Companion Plan pays for covered services up to the Medicare deductibles and coinsurance, the increased Medicare Part A deductible and coinsurance were factors in a Companion Plan rate increase announced for April 1st.

Although the change in Medicare was a major reason for the rate increase, it was not the only one. Increased usage of services and the increased cost of benefits for physicians' services also contributed to the need for an increase.

Therefore, effective April 1, 1978, Companion Plan rates will be going up 16.1%. The new monthly rate for Companion Plan coverage will be $9.75, which will cost subscribers $1.35 more a month.

The Companion Plan contract guarantees that subscribers' coverage will be kept in line with Medicare charges. While this usually does mean a rate increase, it also means more Companion Plan benefits to keep the subscriber's out-of-pocket expenses to a minimum.

Companion Plan will now pay for covered services up to the new $144 deductible (up $20 over last year), the $36 a day coinsurance for the 61st through 90th day (up $5 over last year), and the $72 a day coinsurance for the 91st through 150th day (up $10 over last year).

About 85,000 Maine people are affected by this rate increase.

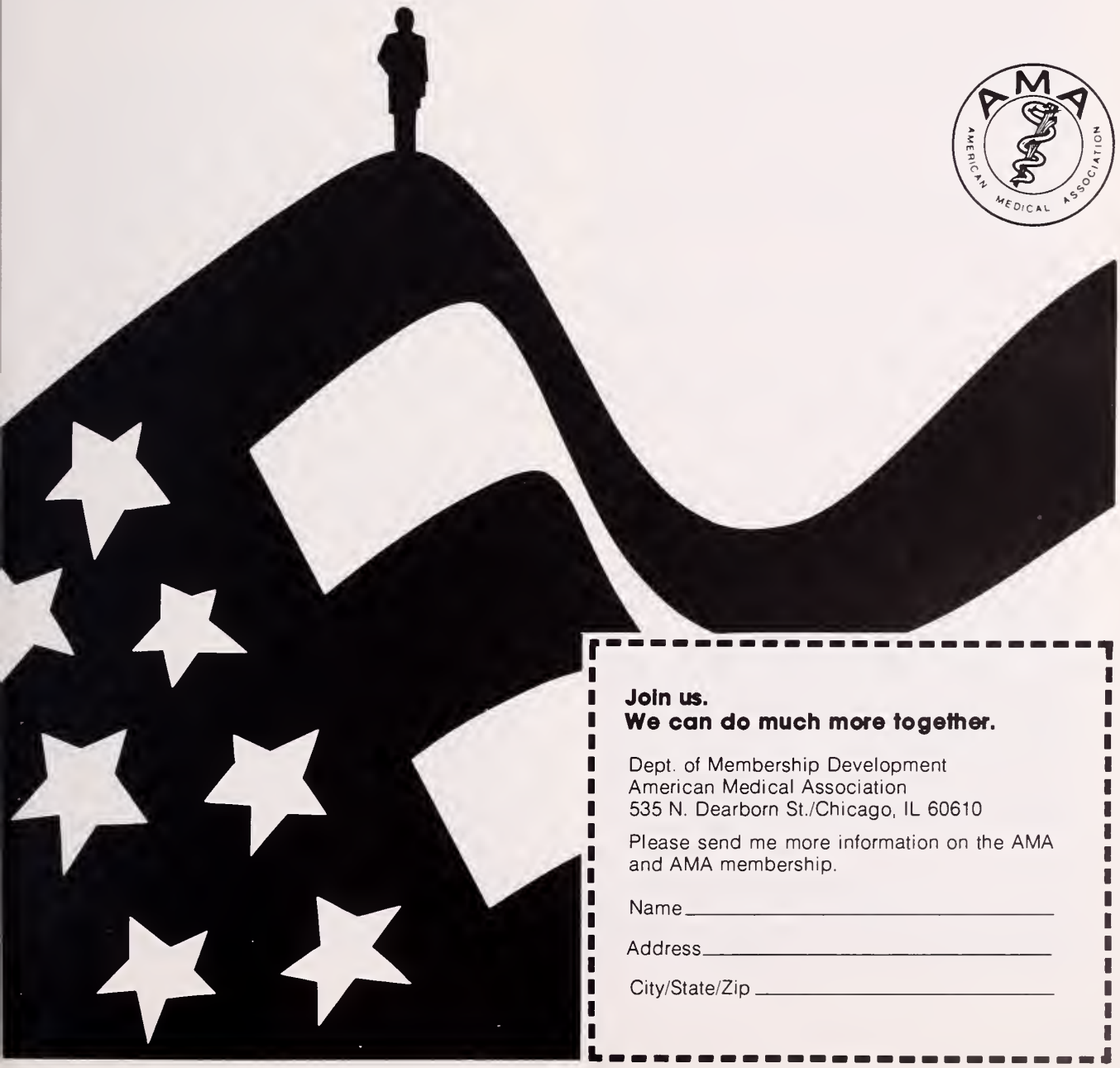
Medicine's men on the Hill

Just who are they? They're the AMA's permanent representatives to the Congress of the United States from the AMA's Washington office.

In every Congress about 10% of all legislation introduced is health related — some 2,500 bills and the number is increasing every year. The AMA lobyists serve as the profession's eyes, ears, and voice on the Hill. Keeping in day-to-day contact with the members of Congress and their staffs. Explaining and promoting the profession's views. Reporting on legislation. And providing legislators with resource material and information on medical and health subjects.

They're on the Hill to protect your interests, lobbying to retain the basic freedoms of medical practice in any government health program that might be enacted. Equally important, they lobby to insure the passage of constructive and workable health legislation for the public.

Sure, the AMA lobbies. It lobbies for the rights and interests of our profession and for quality medical care for every American. With your support, the AMA can be even more effective.



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News, Notes and Announcements

ACP Sponsors Five-Day Postgraduate Course

The American College of Physicians (ACP) will sponsor a five-day postgraduate course "Rheumatic Diseases: Clinical Aspects and Basic Mechanisms," May 15-19, 1978, in Boston, Massachusetts.

The American College of Physicians postgraduate courses have been approved by the American Medical Association Advisory Committee on Continuing Medical Education and the Boston course may be used to fulfill 30 hours of Category #1 requirements for the AMA's Physician Recognition Award.

The course is being planned by the Harvard Medical School and Robert B. Brigham Hospital at Boston, Massachusetts.

For Information and Registration: Registrar, Postgraduate Courses, ACP, 4200 Pine Street, Philadelphia, PA 19104.

A.M.A.'s Medical Leadership Seminar

SEMINAR DATES AND LOCATION: May 26-27, 1978, Plaza Hotel, New York, New York.

ACCREDITATION: 14 credit hours in Category 1 of the Physician's Recognition Award.

REGISTRATION FEE: $150 AMA member or medical society staff; $200 nonmember.

For additional information write or call: American Medical Association, Department of Hospitals and Health Facilities, 535 North Dearborn Street, Chicago, IL 60610 (312)751-6653.

Contemporary Clinical Neurology
July 6-9, 1978

First annual postgraduate course on Hilton Head Island, South Carolina, at the Palmetto Dunes Hyatt Resort

Presented by the Department of Neurology, Vanderbilt University School of Medicine.

Program Chairman: Gerald M. Fenichel, M.D., Professor and Chairman, Department of Neurology; Professor of Pediatrics; Director, Jerry Lewis Neuromuscular Center, Vanderbilt University School of Medicine.

Scientific sessions each day from 8:30 a.m. to 1:00 p.m., on the topics Cerebrovascular Disease, Viral and Demyelinating Diseases, Movement Disorders, and Neuromuscular Disorders.

Accreditation: 16 hours, Category 1, Physicians Recognition Award, American Medical Association.

Registration fee: $200.

For information and registration, contact Vanderbilt Continuing Education, 305 Medical Arts Building, Nashville, TN 37212, Telephone 615-322-2716.

Continuing Medical Education Seminar Series

COURSE TITLE: Coronary Disease, Exercise Testing, and Cardiac Rehabilitation.

SEMINAR DATE AND LOCATION: July 14-16, 1978, Hyannis, Cape Cod, Massachusetts, Dunfey's Lodge.

ACCREDITATION: This continuing medical education offering meets the criteria for 13 credit hours in Category 1 of the Physician's Recognition Award.

REGISTRATION FEE: Physicians: $195; Nurses & Technicians: $95.

COURSE SPONSOR: International Medical Education Corporation, (a non-profit organization), 64 Inverness Drive East, Englewood, Colorado 80110. (800)525-8646 Toll Free.

Aspen Mushroom Conference

Identification of edible, poisonous, and hallucinogenis mushrooms. Treatment of mushroom poisoning. Microscopy. Novice and advanced courses. AMA category 1. August 13-18, 1978. Wildwood Inn, Snow-mass-at-Aspen, Colorado. Contact Beth Israel Hospital, 1601 Lowell Blvd., Denver, Colorado 80204. 303-825-2190 X359.

AAP Kicks Off 1978 Pediatric Journalism Awards Program

The American Academy of Pediatrics has launched its 1978 Pediatric Journalism Awards Program for articles written on the subject of pediatrics from July 1, 1977 through June 30, 1978.

The 1978 program will award $1,000 for the best magazine article and $1,000 each for the best newspaper articles in two separate categories: those newspapers over 100,000 circulation, and those under 100,000 circulation.

The awards will be presented to the winners at the annual meeting of the American Academy of Pediatrics, October 21-26, 1978, in Chicago. Air fare and travel expenses will be provided for the winners. Deadline for submission of entries is July 31, 1978.

For further information, contact: Mr. Ed Kittrell, Jr., Chief, Department of Communications, American Academy of Pediatrics, 1801 Hinman Avenue, Evanston, IL 60204.

New England Regional Burn Program

The *New England Regional Burn Program* (NERBP) has recently been funded by the Department of Health, Education, and Welfare, Division of Emergency Medical Services. This program, one of six demonstration sites in the nation, is responsible for collecting comprehensive data on burn patients seen and treated at hospitals in the Region. The impetus for the program arose from the continuing paucity of adequate baseline data with which to describe the burn injury problem and subsequently to guide and evaluate the delivery of burn care. What is the incidence of burns in the overall population? What is the extent and severity of burn injuries? What is the cost of acute and long-term burn care? What are the social, psychological and emotional impacts of the burn injury on patients and significant others? These and other questions will be examined in greater detail as the data is obtained. Data collection efforts will focus on inpatient records and a sample of emergency department cases. To insure a minimal workload on the part of hospital personnel, all data collection will be accomplished by experienced project staff. Dr. John F. Burke, Chief of Staff, Shriner's Burn Institute, is Project Director. John A. Locke is the Executive Director. Each state in the New England Region has a State Supervisor. For more information, please contact the Maine State Supervisor, Norma Forbrich (207) 622-7566.

Physician Preceptors Needed

If serving as a preceptor to a medical student this summer interests you, please write to Donna M. Knightly, Assistant Project Director, Interdisciplinary Preceptorships, Medical Care Development, Inc., 295 Water Street, Augusta, Maine 04330, or call (207) 622-7566. Students in their preclinical, third, or fourth year are available during July and August. Limited funding possible. Your earliest response will be appreciated as these students are eager to learn about practice in rural Maine.

Letter to the Editor

To the Editor:

Re: Continuing Medical Education Programs, Colby College, Waterville, Maine

Listed below is information about the continuing medical education summer seminars to be held at Colby College this year.

CLINICAL ALLERGY
July 2-6, 1978

OBSTETRICS-GYNECOLOGY
July 5-8, 1978

CURRENT TOPICS IN PEDIATRICS
July 16-20, 1978

SURGICAL TECHNIQUES
July 18-21, 1978

NEUROSURGICAL TECHNIQUES
July 23-27, 1978

OTOLARYNGOLOGY
July 30-August 3, 1978

OFFICE DERMATOLOGY
August 1-4, 1978

OPHTHALMOLOGY
August 6-10, 1978

NUCLEAR MEDICINE
August 13-18, 1978

EPILEPSY COURSE
August 15-18, 1978

FORENSIC MEDICINE
August 20-23, 1978

TOPICS IN PULMONARY DISEASE
August 20-24, 1978

You will note that there are two new programs — the first, in Clinical Allergy with Albert L. Sheffer, M.D., of Harvard Medical School, as director, and the second, in Obstetrics-Gynecology with J. Donald Woodruff, M.D., of Johns Hopkins, as its director. Each of these will provide credit for Category 1 in PRA.

I feel your readers may also be interested in the first annual seminar in Medical and Surgical Emergencies which we will be holding at Colby June 24 and 25. This program is being coordinated by Dr. William Taggart, Director of Emergency Services, Mid-Maine Medical Center in Waterville.

We would also like to bring to your attention that five of our courses have AAFP credit applied for through Dr. Roger Condit. These courses are: Clinical Allergy, Pediatrics, Dermatology, Epilepsy, and Obstetrics-Gynecology.

We would also like to remind your readers that Colby does have accommodations for families and we have a very active social and recreational program during each of the medical seminars.

I am coordinator for all of these programs and if there are any questions, they could be directed to me at Colby College, Waterville, Maine 04901. Thank you very much for all of your help in making these courses known to the physicians of Maine and those on your mailing list.

ROBERT H. KANY, *Director*
Division of Special Programs
Colby College
Waterville, Maine 04901

County Society Notes

Penobscot

The Penobscot County Medical Society met on January 17, 1978. After an excellent dinner at the Helm Restaurant in Bangor, Maine, with about 75 members and guests present, the meeting was opened by the President, Dr. Philip G. Hunter at 8:30 p.m. It was moved and seconded to dispense with the reading of the minutes of the previous meeting as these had been distributed. There being no old or new business to come before the Society, the guests of the evening were introduced.

Dr. Douglas Hill, President of the Maine Medical Association, discussed briefly the certificate of need bill currently before the legislature and asked that we all ask our legislators to vote for the bill that excludes physicians' offices. He mentioned that the malpractice committee is making progress in developing a physician-based malpractice company and should have definite plans to announce by next month. Finally, Dr. Hill mentioned the planned move of the Medical Association office from Brunswick to Augusta. He asked for suggestions from the membership regarding the location and size of the building.

Mr. Charles Cragin, candidate for the Republican nomination for Governor and former lobbyist for the Maine Medical Association, gave a few words of greeting.

The major speaker of the meeting was Dr. Manu Chatterjee, Medical Director of Medical Care Development, Incorporated. He discussed the problems of medical care delivery in the State of Maine and outlined the past and current activities of Medical Care Development, Inc., in reaching a solution to these problems. Four major areas of activity were listed: 1) New methods of solution for rural health care problems. This is exemplified by the Blue Hill/Stonington TV Communication Network and by ambulatory care centers such as the one in Bucksport. 2) Methods of obtaining new health manpower, such as the Central Maine Family Practice Residency which was established with the idea that a medical school would be coming to Maine. Other activities in this area include the family nurse practitioner and pediatric nurse associate programs. 3) Professional and public education. Medical Care Development, Inc. was very active in developing the plans for a medical school and establishing the concept of a Health-Science Center at the University of Maine. An interactive television network has been established in the central part of the State, linking together five hospitals. With regard to public education, this has been aimed mainly at the school health program such as the Yarmouth system. 4) Quality assurance. Activities in this area included rehabilitation standards, cardiovascular standards, and data collection from hospital records.

Current activities of Medical Care Development, Inc. include the experimental ambulatory and rural care programs, professional education such as the compact between the State of Maine and Tufts and the University of Vermont Medical Schools, trying to obtain financing for residency programs and evaluation and implementation of these suggestions in the report of the Chamberlin Committee established by Governor Longley after his veto of the medical school.

Dr. Chatterjee also mentioned that Medical Care Develop-

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ment, Inc. has programs involving other states and is also to a limited degree involved in programs in other countries. He stressed the need for input from the providers of medical care.

Following Dr. Chatterjee's talk, a lively question and answer period was held with several questioners being concerned about the reliability of the statistics that he quoted. It was also pointed out that the image of the medical profession in the eyes of the State legislature is very poor. Dr. Chatterjee stressed the need to improve this image. In response to one question, he admitted that the cost of patient care in the ambulatory care centers is $16.00 per patient encounter. He admitted that this is too high but had no suggestions for lowering it. He also mentioned that in a recent Federal report listing 162 areas in New England which have a shortage of physicians, 121 of these are in the State of Maine.

The meeting was adjourned at 9:30 p.m.

A. MARSHALL SMITH, JR., M.D., *Acting Secretary*

Hancock

The Hancock County Medical Society met at the Hilltop House in Ellsworth, Maine on March 1, 1978, with thirteen members and 10 guests present.

First item of business was election of new officers for the next year:

President: Dr. John R. Tyler, Blue Hill
Vice President: Dr. Ormond L. Hayes, Jr., Bar Harbor
Secretary: Dr. Quinby D. Gurnee, Winter Harbor
Delegate to the M.M.A. House of Delegates: Dr. Chester W. Howe, Blue Hill. Alternate: Dr. Bradley E. Brownlow, Blue Hill

Dr. John D. McIntyre read a letter from Dr. Morris A. Lambdin requesting a leave of absence from the Society during his stay in the Samoan Islands, planned for the next three years. The letter was accepted, pending a check of any problem with leave of absence with membership in the State Association.

A $10.00 check was received and accepted for Drs. Dahl and Chase of the Dahl-Chase pathology group in Bangor, who request a membership in the Hancock County Society, in addition to their Penobscot County Society.

A letter was read from the Committee on Health Care Financing seeking committee members. Dr. Tyler planned to consult with Dr. Winston G. Stewart in Bar Harbor as to whether he might have interest in this regard.

Notices were given as to the Seminar on Negotiations to be held April 1 and 2 in Lewiston. Notice was also given of the Audit Clinic to be held in Augusta on March 9 and 10.

Dr. Randall H. Silver spoke on the Downeast Health Services and he requested physicians to be represented on the board of directors to be selected in July. Dr. John C. Van Pelt moved that at the next County meeting we nominate representatives to this board. The motion was seconded by Dr. Bradley E. Brownlow and passed unanimously.

The evening concluded with a very interesting and informative discussion of the development of the "Physicians Mutual Insurance Company of Maine" by the speaker, Dr. Patrick A. Dowling of Portland. The group was very interested in this development and asked many questions following the address by the speaker.

The meeting was adjourned with future meetings to be planned by the new executive committee.

WILLIAM C. BROMLEY, M.D., *Secretary*

CORRECTIONS

DOPAMINE INDUCED GANGRENE — In the February 1978 issue of The Journal, the dose of dopamine on page 47, paragraph 4, line 4 should read 50-60 *micrograms* and not 50-60 mg/kg/minute. The Front Cover identifies one of the authors, Martin Keibel, M.D., as coming from Lewiston. Dr. Keibel is a Resident at the Central Maine Family Practice Residency Program in Augusta.

Librax®
Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br.

Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCl and/or clidinium Br.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants, and against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Physical and psychological dependence rarely reported on recommended doses, but use caution in administering Librium® (chlordiazepoxide HCl) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) reported following discontinuation of the drug.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy. Advise patients to discuss therapy if they intend to or do become pregnant.**

As with all anticholinergics, inhibition of lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established.

Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated; avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, *i.e.*, dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

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County Society Notes

York

The annual meeting of the York County Medical Society was held on January 11, 1978 at the Kennebunk Inn, Kennebunk, Maine.

The social hour was held from 6:30 to 7:30 p.m.

After an excellent dinner, a most interesting and informative talk was given by State Senator Walter W. Hichens of Eliot, Maine. His subject was "Health Legislation of Concern to Maine Physicians."

Following his speech, Dr. Lawrence Hazzard, President of our Society, called the business meeting to order. The first item on the agenda, was a report of the Nominating Committee concerning their choice of Officers and Committees, for the ensuing year 1978.

These include the following:

President: Dr. Lawrence R. Hazzard, York

Vice President: Dr. Michael M.P. Magaudda, Old Orchard Beach

Secretary-Treasurer: Dr. Melvin Bacon, Sanford

Executive Committee: Drs. Walter R. Peterlein, Jr., Springvale and Robert S. LaFond, Saco (plus the above officers)

Delegates to the M.M.A. House of Delegates: Drs. Carl E. Richards, Alfred, Robert F. Ficker, Kennebunkport and Lyman A. Page, Saco. Alternates: Drs. Alvin A. Hoffman, York, Michael M.P. Magaudda, Old Orchard Beach and Robert D. Vachon, Sanford

Census Committee: Drs. Marion K. Moulton, W. Newfield, Roger J.P. Robert, Biddeford and Paul S. Hill, Jr., Saco

Peer Review Committee: Drs. Kenneth E. Leigh, York, Harry Lapirow, Kennebunk and Conner M. Moore, Saco

Nominating Committee for 1979: Drs. Melvin Bacon, Sanford, John H. Leonard, York and Carl M. Haas, Biddeford

Following a request from the Maine Medical Association, for three members from the York County Medical Society, to serve on its arbitration panel, the three following physicians were also nominated: Drs. Kenneth E. Leigh, York, Vincent J. Hickey, Biddeford and Marion K. Moulton, W. Newfield.

All the afore mentioned were unanimously elected to serve for year 1978.

The minutes of the October meeting were dispensed with, in the interest of time.

The next item on the agenda was a brief Financial Report for 1977. It was announced that we are financially solvent, that the expenses were kept at a minimum and that no increase in dues was anticipated.

There was no old business to be discussed.

New business involved the election to membership to our Society. These included Drs. Terrence Horrigan, Edward Holland, and Lawrence Golodner, a transfer from Aroostook County.

Continued on Page 159

Physician Preceptors Needed

If serving as a preceptor to a medical student this summer interests you, please write to Donna M. Knightly, Assistant Project Director, Interdisciplinary Preceptorships, Medical Care Development, Inc., 295 Water Street, Augusta, Maine 04330, or call (207) 622-7566. Students in their preclinical, third, or fourth year are available during July and August. Limited funding possible. Your earliest response will be appreciated as these students are eager to learn about practice in rural Maine.

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Officers of the Maine Medical Association — 1977-1978

President, Douglas R. Hill, M.D., South Portland

President-elect, Francis I. Kittredge, M.D., Bangor

Speaker of the House of Delegates, George W. Bostwick, M.D., Newcastle

Vice Speaker of the House of Delegates, A. Dewey Richards, M.D., Orono

		Term Expires
Executive Committee Members		
Maurice Ross, M.D., Saco	First District—York	1979
William H. Maxwell, M.D., Portland	Second District—Cumberland	1978
John W. Wickenden, M.D., Rockland	Third District—Lincoln-Sagadahoc, Knox	1980
Executive Committee Chairman		1978
O. Thomas Feagin, M.D., Augusta	Fourth District—Kennebec	1978
David L. Phillips, M.D., Rumford	Fifth District—Franklin, Oxford, Somerset	1979
Harold E. Knuuti, M.D., Belfast	Sixth District—Hancock, Washington, Waldo	1979
Gilbert R. Grimes, M.D., Lewiston	Seventh District—Androscoggin	1980
Charles H. Lightbody, M.D., Guilford	Eighth District—Penobscot, Piscataquis	1980
Eric F. Nicholas, M.D., Mars Hill	Ninth District—Aroostook	1978
Richard C. Leck, M.D., Bath	Immediate Past President	1978
Robert E. McAfee, M.D., Portland	Delegate to the AMA	Dec. 31, 1979
Brinton T. Darlington, M.D., Augusta	Alternate Delegate to the AMA	Dec. 31, 1979
Daniel F. Hanley, M.D., Brunswick	Executive Director	

Assistant Executive Director, Mr. D. Jeffrey Hollingsworth, Brunswick

Secretary-Treasurer, Patricia A. Bergeron, Brunswick

Association and Journal Headquarters

Dudley Coe Infirmary, College Street, Brunswick, Maine 04011

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The Journal of the Maine Medical Association

Volume Sixty-nine | Brunswick, Maine, May 1978 | Number 5

Program – 125th Annual Session
Maine Medical Association

June 10, 11, 12, 13, 1978

Treadway-Samoset, Rockport

Arranged by the Scientific Committee

HAROLD N. BURNHAM, M.D., Gorham
Chairman

GEORGE E. DAVIS, JR., M.D., Augusta

DON L. MAUNZ, M.D., Bangor

DAVID G. REED, M.D., Camden

DANA M. WHITTEN, M.D., Belfast

Dr. Burnham

The Scientific Program of the annual meeting of the Maine Medical Association is made possible by the cooperation and assistance of the Technical Exhibitors and the following organizations:

Maine Medical Center
Portland, Maine

Tufts University School of Medicine
Boston, Massachusetts

Merck Sharp & Dohme Postgraduate Program
West Point, Pennsylvania

Maine Chapter, American Academy of Family Physicians

Maine Chapter, American College of Surgeons

Maine Medico-Legal Society

Maine Trauma Committee

Blackwell's Surgical and Orthopedic Appliances
Portland, Maine

Bristol Laboratories
Syracuse, New York

Brunswick Publishing Company
Brunswick, Maine

Eli Lilly and Company State Medical Convention Program
Indianapolis, Indiana

Maine Blue Cross and Blue Shield
Portland, Maine

Maine Pharmaceutical Association

Parke, Davis & Company
Detroit, Michigan

E. R. Squibb & Sons, Inc.
Princeton, New Jersey

Treadway-Samoset Resort
Rockport, Maine

Specialty Groups

Maine Society of Allergy and Immunology

Maine Society of Pathologists

Maine Chapter, American Academy of Pediatrics

Maine Psychiatric Association

Maine Thoracic Society

Maine Urologic Association

Information

Registration:
Registration throughout the session will be in the Lobby at the Treadway-Samoset.
Saturday, June 10 — 12:00 M. to 5:00 P.M.
Sunday, June 11 — 8:30 A.M. to 5:00 P.M.
Monday, June 12 — 8:30 A.M. to 5:00 P.M.
Tuesday, June 13 — 8:30 A.M. to 3:00 P.M.

Telephone: The number at the Treadway-Samoset is Rockport, (207) 594-2511.

Meal Tickets:
For those not registering in the hotel, meal tickets must be purchased in advance by using the hotel reservation form.

Visiting Delegates:
Introduction of Visiting Delegates will take place at meetings of the House of Delegates on Saturday, June 10 and Sunday, June 11.

Technical Exhibits:
This year, seventeen companies are contributing to the success of the annual session program by participating in the Technical Exhibits. A list of the exhibiting companies and representatives will be found on page 141 of this program.
Please show your appreciation for the support of these companies by visiting these exhibits.

Badge Code:
Badges with green borders indicate Officers, Past Presidents, Delegates and Alternate Delegates of the M.M.A.; yellow borders, members of the M.M.A.; blue borders, guests; red borders, exhibitors; and plain white for the members of the Auxiliary.

Saturday, June 10

2:00 P.M. First Meeting of the House of Delegates

Call to Order: DOUGLAS R. HILL, M.D., President

Presiding: Speaker of the House, GEORGE W. BOSTWICK, M.D.

Presentation of the A. H. Robins' Physician Award for Community Service

Presentation of the Maine Blue Cross and Blue Shield "Award of Appreciation"

6:30 P.M. COCKTAILS (Cash Bar)

7:30 P.M. DINNER

ENTERTAINMENT: RUSS BURGESS — **"ESP in Action"**

Dancing in the Hotel's Lounge

Sunday, June 11

7:30 to 9:00 A.M. BREAKFAST

8:30 A.M. Reference Committee Meetings

12:00 M. LUNCHEON

2:00 P.M. Second Meeting of the House of Delegates

Election of President-elect and Executive Committee District Members

6:00 P.M. COCKTAILS (Cash Bar)

7:00 P.M. **Lobster Bake**

Speaker: ROBERT B. HUNTER, M.D., Chairman, Board of Trustees, American Medical Association

ENTERTAINMENT: **Dancing to the DON DOANE BAND**

Monday, June 12

7:30 to 9:00 A.M. BREAKFAST

Scientific Program

"ABOVE ALL, DO NO HARM"

9:00 A.M. to 12:00 M.

Welcome — DOUGLAS R. HILL, M.D.

Presented by the Maine Medical Center, Portland

9:00 A.M. Welcome and Introductions

HAROLD N. BURNHAM, M.D., Chairman, M.M.A. Scientific Committee

9:10 A.M. **"Ultrasound: A Less Invasive Alternative"**

Speaker:

ANTHONY F. SALVO, M.D., Director, Division of Ultrasound, Department of Radiology, Maine Medical Center, Portland

10:00 A.M. **"Physicians' Primer on Environmental Disease"**

JOHN M. PETERS, M.D., Sc.D., Professor, Occupational Medicine and Director, Occupational Health Program, Harvard School of Public Health

Dr. Peter's Presentation is Co-sponsored by the Maine Society of Allergy and Clinical Immunology and the Maine Thoracic Society

10:50 A.M. INTERMISSION

11:00 A.M. **"The Doctor as an Anxiety-Ogenic and Anxiety-Olytic Agent"**

Moderator — STEPHEN M. SOREFF, M.D., Director, Emergency and Consultation Psychiatry, Maine Medical Center, Portland

Speakers:

AKE AKERBERG, M.D., Psychiatrist, Lewiston

WILLIAM J. BARNUM, M.D., Director, Mid-Coast Community Mental Health Center, Rockland

NANCY M. COYNE, M.D., Psychiatrist, Augusta

RICHARD DALY, M.D., Psychiatrist, Bangor

12:00 M. LUNCHEON

Scientific Program

"ABOVE ALL, DO NO HARM"

2:00 to 4:30 P.M.

Welcome — GEORGE E. DAVIS, JR., M.D.

Presented by Tufts University School of Medicine, Boston

2:00 P.M. **"The Role of Immediate Postoperative Prosthetics in Amputee Management"**

PAUL J. CORCORAN, M.D., Associate Professor and Chairman, Department of Physical and Rehabilitative Medicine, Tufts University School of Medicine and Psychiatrist-in-Chief, Rehabilitation Institute, Tufts-New England Medical Center Hospital

2:40 P.M. **"Pediatrics Without the Laboratory"**

MAURICE A. KIBEL, F.R.C.P., D.C.H., Visiting Professor in Pediatrics, Tufts University School of Medicine

3:30 P.M. **"Non-Invasive Approaches to Cardiovascular Disease"**

JOHN S. BANAS, JR., M.D., Associate Professor of Medicine, Tufts University School of Medicine and Director, Adult Cardiovascular Laboratory, Tufts-New England Medical Center Hospital

6:00 P.M. RECEPTION

7:00 P.M. **Annual Banquet**

Presentation of Honorary Pins

President's Address: DOUGLAS R. HILL, M.D.

ENTERTAINMENT: **"America's Spirit"** — The Hyde School, Bath, Maine

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Tuesday, June 13

7:30 to 9:00 A.M. BREAKFAST

Scientific Program

9:00 A.M. to 12:00 M.

Welcome — DANA M. WHITTEN, M.D.

Presented by the Maine Medical Center, Portland

"SURGERY UPDATE"

Moderator — RICHARD C. BRITTON, M.D.

"Management of Hiatal Hernia and Gastroesophageal Reflux: 20 Years Experience"

CLEMENT A. HIEBERT, M.D., Thoracic Surgeon, Portland

"Present Status of Coronary By-Pass Surgery"

JEREMY R. MORTON, M.D., Thoracic Surgeon, Portland

"Report on Maine Burn Program"

RICHARD C. BRITTON, M.D., Chief of Surgery, Maine Medical Center, Portland

"Update on Vascular Surgery"

FERRIS S. RAY, M.D., Director, Division of Vascular Surgery, Portland

"Pediatric Surgery in Maine"

MICHAEL R. CURCI, M.D., Pediatric Surgeon, Portland

"Solving the Problem of the Retained Postoperative Gallstone"

ANDREW B. PACKARD, M.D., Associate Radiologist, Portland

GEORGE F. SAGER, M.D., General Surgeon, Portland

"What's New in Arthroscopy"

LAWRENCE CRANE, M.D., Orthopedic Surgeon, Portland

Question and answer period

12:00 M. LUNCHEON

Scientific Program

2:00 to 4:00 P.M.

Welcome — DAVID G. REED, M.D.

Co-sponsored by the Maine Medico-Legal Society

"Gross Therapeutic Misadventures" and "Interesting Cases in Forensic Pathology"

MARVIN E. ARONSON, M.D., Chief Medical Examiner, City of Philadelphia

Specialty Group Meetings

Monday, June 12

1:00 P.M. **MAINE THORACIC SOCIETY**

2:00 P.M. **MAINE UROLOGIC ASSOCIATION**
ANDREW P. IVERSON, JR., M.D., Portland, presiding

Tuesday, June 13

12:00 NOON — Main Dining Room

INFORMAL LUNCHEON

Maine Society of Pathologists

2:00 P.M. **MAINE CHAPTER, AMERICAN ACADEMY OF PEDIATRICS**

GEORGE W. HALLETT, M.D., Portland, presiding

Business Meeting

2:00 P.M. **MAINE PSYCHIATRIC ASSOCIATION**

STEPHEN M. SOREFF, M.D., Portland, presiding

"How Psychotherapy Heals"

JEROME D. FRANK, M.D., Professor Emeritus of Psychiatry, Johns Hopkins University School of Medicine, Baltimore

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Special Notices

A.A.F.P. Prescribed Credit
This program is approved for 10 Prescribed Hours by the American Academy of Family Physicians.

M.M.A. Credit for Category I
The Monday and Tuesday regular scientific sessions are accepted for 10 hours credit (1 credit per hour) in the Physicians Recognition Award Category I.

Executive Committee Meetings
The Executive Committee will meet on Saturday, June 10 and daily throughout the session at a time and place to be announced.

PTO-PSRO — Annual Meeting
Monday, June 12 — 1:30 P.M.
Open to all physicians

HONORARY PINS

Presentation of the Association's Honorary Pins will be made by Douglas R. Hill, M.D., President of the M.M.A., at the Annual Banquet, Monday evening, June 12 at 7:00 P.M.

FIFTY-YEAR LAPEL PINS

Fifty-Year Lapel Pins will be presented to the following members who were graduated from Medical School in 1928:

Androscoggin County
Camille Tousignant, M.D.
Medical College of Georgia

Franklin County
Harry Brinkman, M.D.
University of Michigan Medical School

Penobscot County
Asa C. Adams, M.D.
University of Vermont College of Medicine

Waldo County
Raymond L. Torrey, M.D.
Northwestern University Medical School

FIFTY-FIVE-YEAR LAPEL PINS

Fifty-Five-Year Lapel Pins will be presented to the following members who were graduated from Medical School in 1923:

Androscoggin County
Charles F. Branch, M.D.
University of Vermont College of Medicine

Cumberland County
Abram I. Cohen, M.D.
Tufts University School of Medicine

Theodore M. Stevens, M.D.
Harvard Medical School

Kennebec County
Howard F. Hill, M.D.
Harvard Medical School

Knox County
Barbara B. Stimson, M.D.
Columbia University College of Physicians and Surgeons

Oxford County
Chesley W. Nelson, M.D.
University of Vermont College of Medicine

York County
Herman G. Sandvoss, M.D.
University of Munich

SIXTY-YEAR LAPEL PINS

Sixty-Year Lapel Pins will be presented to the following members who were graduated from Medical School in 1918:

Knox County
Harry A. Naumer, M.D.
Columbia University College of Physicians and Surgeons

Penobscot County
W. Merritt Emerson, M.D.
University of Vermont College of Medicine

SIXTY-FIVE-YEAR LAPEL PINS

Sixty-Five-Year Lapel Pins will be presented to the

following members who were graduated from Medical School in 1913:

Androscoggin County
Ralph A. Goodwin, Sr., M.D.
Harvard Medical School

Cumberland County
Albert W. Moulton, Sr., M.D.
Bowdoin Medical School

29th Annual Meeting

Auxiliary to the Maine Medical Association

Open to All Physicians' Wives

Monday, June 12

9:00 A.M. to 12:00 M. Registration
Lobby, Treadway-Samoset, Rockport

9:30 to 10:15 A.M. Open House Coffee
Boutique II

10:15 A.M. House of Delegates Annual Business Meeting
Boutique II
MRS. JAMES SMITH, President, presiding

12:00 to 12:30 P.M. Reception
Ebb Tide Room

12:30 P.M. Annual Luncheon in Honor of Past Presidents of the Auxiliary to the M.M.A.
Welcome — Convention Hostess

2:00 P.M. Adjournment

2:15 P.M. 1978-1979 Board of Directors Meeting
North Samoset Room

"Medicine Avenue"

Technical Exhibits

Astra Pharmaceutical Products, Inc., Pleasant Street Connector, Framingham, Massachusetts 01701

Boehringer Ingelheim Ltd., 90 East Ridge, P. O. Box 368, Ridgefield, Connecticut 06877

Burroughs Wellcome Co., 3030 Cornwallis Rd., Research Triangle Park, North Carolina 27709

Dow & Pinkham, Div. of Morse, Payson & Noyes, 57 Exchange St., Portland, Maine 04112
Representatives: Mr. Richard H. Pew, Jr., Mrs. Linda W. Myers and Mr. Frederick A. Prince, C.L.U.

Lederle Laboratories, A Division of American Cyanamid Company, Pearl River, New York 10965
Representatives: Mr. R. Maffei, Mr. S. Keniston, Mr. R. Hayman, Mr. P. DeCotis and Mr. H. Heili

Maine Blue Cross and Blue Shield, 110 Free St., Portland, Maine 04101
Representatives: Mrs. Laura Franciose, Shirley M. Brochu, R.N., Ms. Beth Walker, Ms. Dale McNelly, Ms. Agnes Costello and Ms. Elinor Plaisted

Maine National Bank, 400 Congress St., P. O. Box 919, Portland, Maine 04104
Representatives: Ms. Barbara Weldon, Mr. Thomas Acker and Ms. Gail C. Foust

McNeil Laboratories, 500 Office Center Dr., Fort Washington, Pennsylvania 19034
Representatives: Mr. Joe Ruest and Mr. Ron Clash

Mead Johnson Laboratories, 2404 W. Pennsylvania St., Evansville, Indiana 47721
Representative: Mr. Remi St. Onge

Pfizer Laboratories Division, Pfizer Inc., 230 Brighton Rd., Clifton, New Jersey 07012
Representatives: Mr. Joe Maioriello, Mr. Charles Jankoski and Mr. Jerry Dorsky

Phi Data Inc., 2001 Upper Hammond St., Bangor, Maine 04401
Representatives: Mr. Edward F. Lucia, Jr., Mr. Jeffrey S. Ross and Mr. Kenneth P. Meuse

Reed & Carnrick Pharmaceuticals, Kenilworth, New Jersey 07033

A. H. Robins Company, 1407 Cummings Dr., Richmond, Virginia 23220
Representative: Mr. Hubert Strom

William H. Rorer, Inc., Fort Washington, Pennsylvania 19034
Representatives: Mr. Alfred L. Vogler, Mr. Robert W. Roffler and Mr. James H. MacDonald

Sandoz Pharmaceuticals, East Hanover, New Jersey 07936
Representatives: Mr. Larry Emidy and Mr. Wayne Jackson

Searle Laboratories, Div. of G. D. Searle & Co., Box 5110, Chicago, Illinois 60680
Representatives: Mr. Daniel Arimento, Mr. Alfred Grimes and Mr. A. James Allott

U. S. Army Medical Department Personnel Support Agency, Department of the Army, Washington, D.C. 20324
Representatives: Captain Peter Tremblay and Captain Richard Griswold

Special Exhibits

American Cancer Society, Maine Division, Inc.

Disability Determination Service

Section on Ophthalmology of the M.M.A.

Visiting Delegates

The Connecticut State Medical Society
W. Raymond James, M.D., Essex

Medical Society of the State of New York
Ralph S. Emerson, M.D., Roslyn Heights

Delegates to Out-of-State Meetings

The Connecticut State Medical Society
George W. Bostwick, M.D., Newcastle

The Massachusetts Medical Society
Nelson P. Blackburn, M.D., Bath

Medical Society of the State of New York
Douglas R. Hill, M.D., South Portland

The Rhode Island Medical Society
Leonard G. Miragliuolo, M.D., Bangor

Vermont State Medical Society
Robert F. Ficker, M.D., Kennebunkport

County Delegates

DELEGATES	ALTERNATES
Androscoggin County Medical Association	
Kenneth P. Wolf, M.D., Secretary	
Thomas F. Shields, M.D.	Mary T. Dycio, M.D.
Behzad Fakhery, M.D.	Margaret H. Hannigan, M.D.
Frederick C. Holler, M.D.	Ake Akerberg, M.D.
Stephen A. Sokol, M.D.	Barry D. Chandler, M.D.
Lawrence A. Nadeau, M.D.	Donald H. Morgan, M.D.
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Care of the Dying — A Country Doctor Speaks Out

E. STANLEY YOUNG, M.D.

A great deal has been written in recent years about care of[1-42] the dying, both from the medical and ethical points of view. As a medical student, intern and primary care practitioner, I have been involved in the care of dying patients since 1956. My personal philosophy regarding prolongation of life has evolved unencumbered by formal instruction.

What is the role of the physician? It is to act in the best interests of his patient. Does this always mean using all available modes of treatment to prolong life? I think not. Clinical situations frequently arise in which there is no hope for rehabilitation or return to an acceptable quality of life. Many physicians feel that they are not qualified to make "quality of life" decisions for a patient. I disagree. Making this kind of decision is an important role of the physician, and leads naturally to more humane care of the dying, and a role more supportive to the family of the dying patient.

The country doctor is frequently friend as well as physician to his patients. On a given day, he may be faced with making the decision that it is no longer in the patient's best interest to prolong life, but that the goal of therapy now is to provide the patient with a quick and comfortable mode of dying.

What are the guidelines by which the physician is to act? I suggest two simple rules of conduct. First, one must be guided by the rule of common sense, and second by the "Golden Rule", that is to say, to treat the patient as you would wish to be treated were the roles reversed. Some of my physician colleagues challenge this latter concept on the grounds that family members are better qualified to make "quality of life" decisions for the patient who can no longer speak for himself. One should recognize, however, that a family member may be guided by motivations that do not reflect the character of the patient.

Certain practical, legal and political considerations may temper the actions of the physician. Local community standards of practice must be taken into account.

How, then, should a physician come to the decision to change patient management from supportive to symptomatic? In some cases the patient may be able to request this change. Even the comatose patient may have made his desires clear in a premorbid statement such as a "Living Will" provided by the Euthanasia Council. If the patient is unable to take part in decision-making, the physician may consult with family or guardian in a supportive way that will minimize guilt feelings when the outcome is a decision to withhold treatment.

Frequently family may insist on continued treatment which the physician feels is not in the best interest of the patient. In this situation, the physician must frequently acquiesce to family demands in order to protect his own reputation and legal safety.

The physician may rest easy, however, if he has done his best as advocate for the patient. Despite any legal and political hazards encountered along the way, the physician has primarily his own conscience to answer to in the long run.

Certain third parties with vested interests may sometimes try to influence the doctor-patient relationship. Of particular note is the fact that a proprietary nursing home may have a vested interest in keeping a given patient alive because he is a superior source of income. This policy is mentioned in passing only to condemn it.

What manner of patients may be considered for symptomatic treatment? A few of many discussed in the referenced papers are (1) those with terminal cancer; (2) those with severe chronic brain syndrome and other degenerative neurologic diseases; (3) severe mental defectives; (4) neonates with severe physical anomalies which preclude survival; and (5) patients with terminal cardiopulmonary conditions.

A fine distinction of judgment may determine in a given situation whether an action by the physician is science at its best or medical meddling.

What are some of the treatments which may be withheld to reach a therapeutic goal? I suggest that a few are:

(1) withholding antibiotics for infection.
(2) withholding fluid and electrolyte replacement.
(3) withholding blood replacement.

Positive steps toward "good death" revolve around the use of adequate sedation and analgesia.

Who shall decide these difficult issues? In the long run it will not be the medical profession, nor the legal profession, nor the clergy. Public opinion will decide these issues as it does in all matters pertaining to folkways.

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Drug Therapy of Glaucoma

DONALD P. DURKEE and BOBBY G. BRYANT, Pharm.D.

Glaucoma is an ocular disease characterized by abnormally elevated intraocular pressure. It is responsible for 10 to 20% of cases of blindness in the United States.[1] Descriptions of the disease appeared in written history as early as the first few centuries A.D., but it was not until the 19th century that the concept of increased intraocular pressure in glaucoma became well established.[2]

OCULAR PHYSIOLOGY

The eyeball is a hollow sphere protected by a tough outer coat of connective tissue. The white sclera constitutes the posterior portion of this tissue and the transparent cornea, the anterior portion. A gelatinous mass (known as the vitreous humor) enclosed in a fine membrane fills the posterior four-fifths of the eye. The sclera and the vitreous humor help to maintain the structure of the eye (Figure 1).

The lens, iris, and ciliary body are located in the anterior fifth of the eye. The lens acts as a fine adjustment to sharpen the focus of images coming into the eye. The iris regulates the amount of light entering the eye by constricting or dilating the pupil. The ciliary body secretes a watery fluid, called the aqueous humor, which circulates around the lens (behind the iris), through the pupil, and into the space between the iris and cornea, termed the anterior chamber. The aqueous humor then filters through a sieve-like opening known as the trabecular network and into Schlemm's canal, a circular space that passes all the way around the eye at the junction of the sclera and cornea. The trabecular network is located in the angle formed at the point where the outside edge of the iris attaches to the cornea. The aqueous humor is then returned to the circulation via the aqueous veins which empty into the venous blood vessels of the eye. The continuous flow of aqueous humor is necessary to maintain normal intraocular pressure and support the metabolism of the lens, which does not have a blood supply of its own. Any obstruction to the outflow of aqueous humor or excess production of this fluid will cause intraocular pressure to rise.

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Increases in intraocular pressure are transmitted directly to the capillaries of the retina and the optic nerve. This pressure can cause atrophy and collapse of these capillaries, leading to insidious ischemia and a gradual loss of peripheral vision and eventual blindness if the pressure is not controlled.[3-5]

Normal intraocular pressure is 10 to 20 mmHg. Diurnal fluctuations in the pressure are generally 3 to 4 mmHg with the highest pressure occurring in the morning and the lowest in the evening. This fluctuation may be reversed or more complex in certain individuals.[6,7] Intraocular pressure can be determined by tonometry, a procedure that measures the resistance of the cornea to indentation by a tonometer. When intraocular pressure is increased, indentation is more difficult and a higher reading results.[4]

CLASSIFICATION OF GLAUCOMA

Glaucoma is divided into three main categories based on the cause of the increased intraocular pressure.[2]

I. Primary glaucoma — not due to obvious disease of the eye.
   - A. Narrow-angle glaucoma — also called angle-closure, closed-angle, iris block, congestive, acute, or uncompensated glaucoma.
   - B. Open-angle glaucoma — also called simple, chronic, compensated, or wide-angle glaucoma.

II. Secondary glaucoma — due to preexisting ocular disease.
   - A. Associated with pupillary block.
   - B. Not associated with pupillary block.
   - C. Associated with intraocular inflammation.
   - D. Associated with trauma.

III. Congenital glaucoma — due to obstruction of drainage by congenital anomalies.

Primary glaucoma is by far the most common type. It can occur in infants, children, and young adults, but its incidence increases markedly in persons over 40 years of age. It occurs in 1 to 2% of the population over 40 years and increases 5 to 9% in people over 65 years. Open-angle glaucoma accounts for 90% of the cases of primary glaucoma while narrow-angle is responsible for less than 5% of the cases.[1,3]

NARROW-ANGLE GLAUCOMA

In narrow-angle glaucoma, the eye typically has a

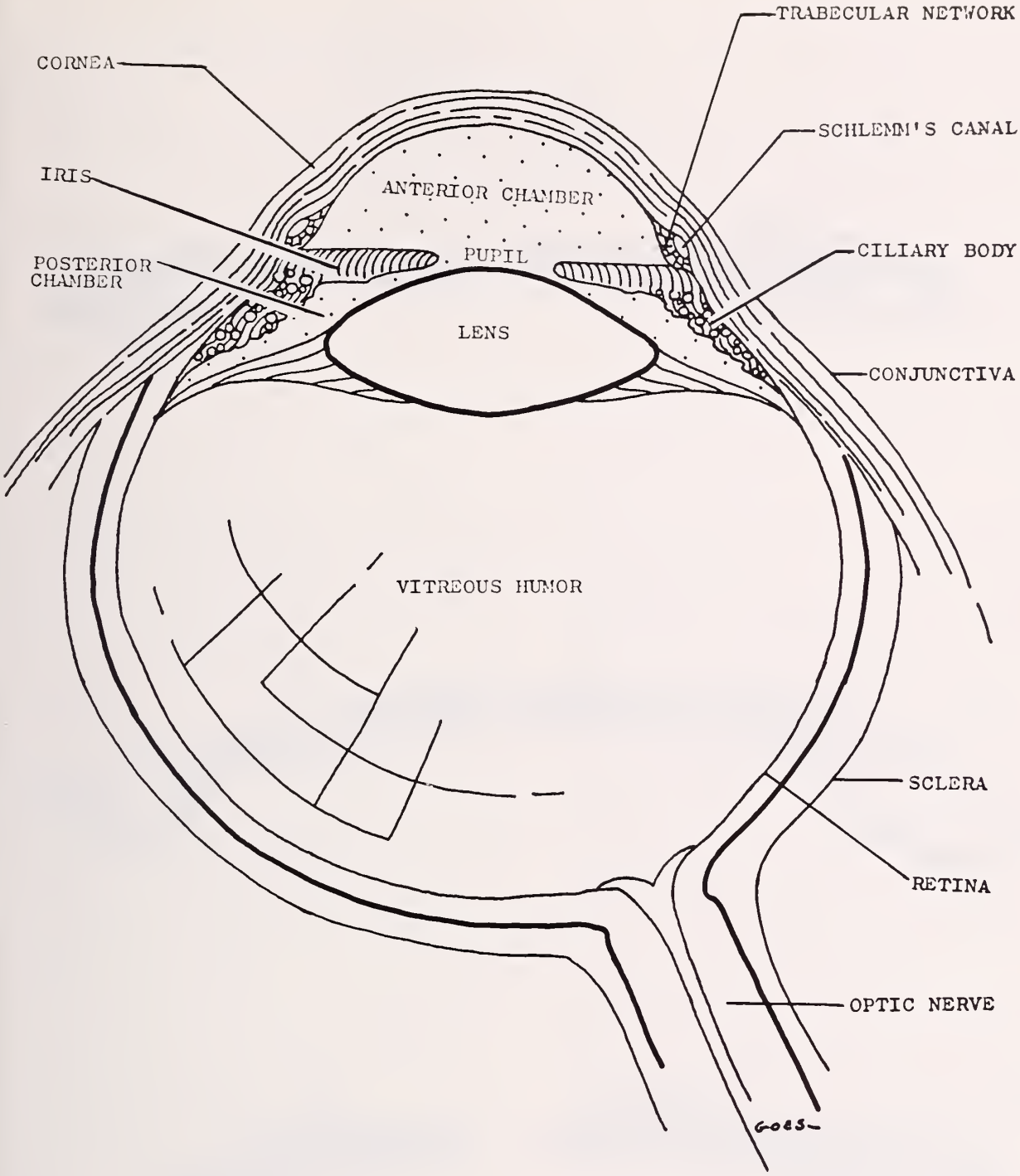

Fig. 1. The human eye.

shallow anterior chamber which forms a narrow angle at the point where the outside edge of the iris is attached to the cornea. This shallow chamber, apparently an inherited trait, is due to the anterior lens surface being relatively close to the cornea. The abnormality of the chamber could result from an increased thickness of a normally positioned lens, a forward displacement of the entire lens, or a combination of both. The close placement of the lens to the cornea forces the iris to bow forward, placing the outer edge of the iris in close proximity to the trabecular network, where Schlemm's canal is located[2] (Figure 2).

In patients with extremely narrow angles, increased intraocular pressure can occur when the periphery of the iris moves forward, such as in pupil dilation. A more common mechanism of narrow-angle glaucoma is pupillary block which can occur with minimal pupil dilation in a patient with a shallow anterior chamber. The forward position of the

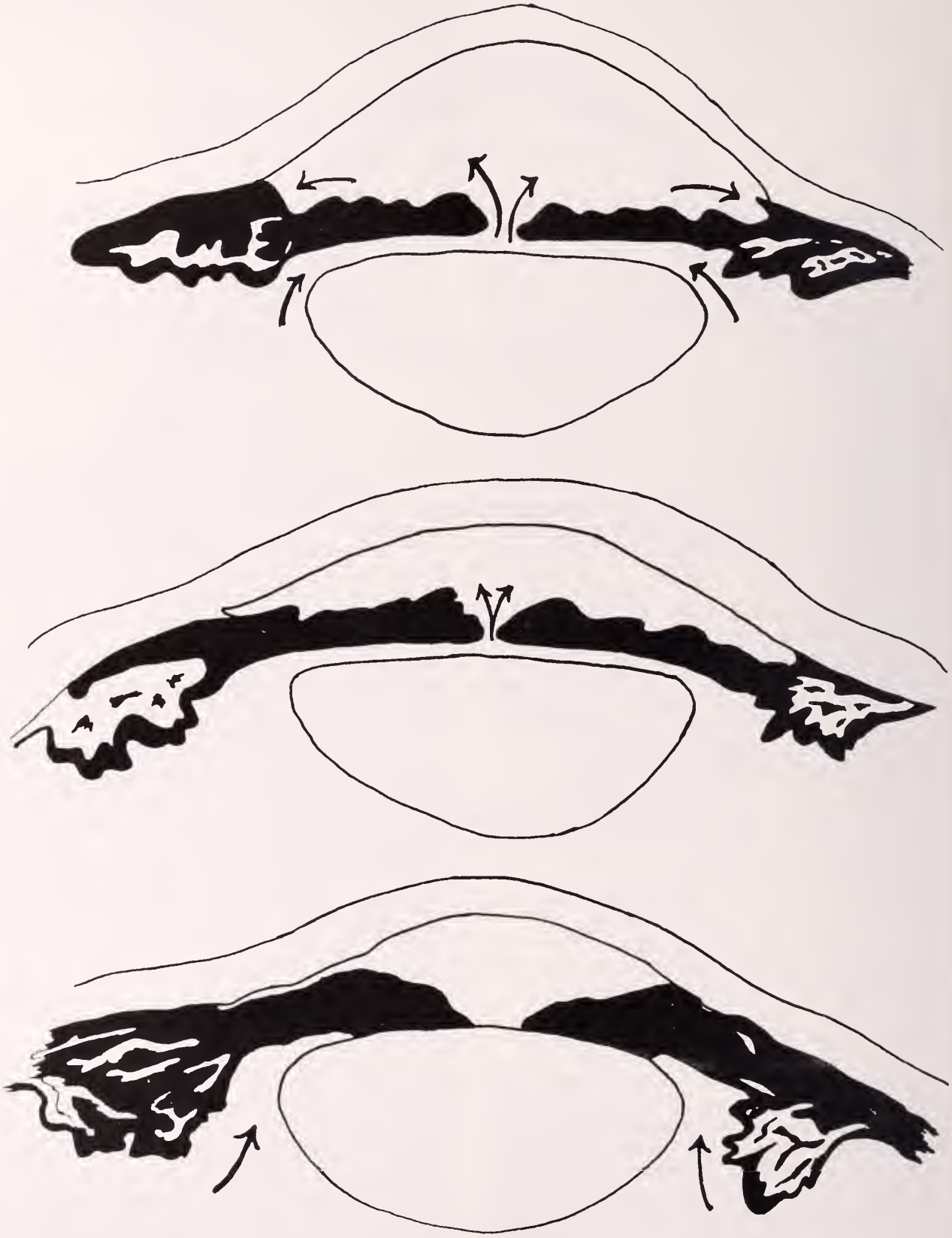

Fig. 2. *Top:* Normal anterior chamber with wide angle. *Middle:* Shallow anterior chamber, with narrow, but open angle. The intraocular pressure would be normal in this eye. *Bottom:* In the narrow-angled eye, pupillary block or pupillary dilation may cause angle closure, blocking the outflow of aqueous humor and resulting in increased intraocular pressure.

Table 1

Commonly Used Hyperosmotic Agents in the Management of Narrow-Angle Glaucoma

Drug	*Comments*
Mannitol (Osmitrol) Dose: Adults: 1.5 to 2 g/kg Children: 1.5 g/kg	Must be given intravenously over 30 to 40 minutes. In adults use 20% solution. In children use 5 to 10% solution. Maximum effect in one hour, may persist for 5 to 6 hours. Can be used in patients with renal disease. Less local reaction produced than with urea. Side effects include headache, dizziness, nausea, hypokalemia, fluid overload. NOTE: Mannitol solutions (especially 20%) tend to crystallize at cooler temperatures; they may be redissolved by warming in a water bath. Be sure solution cools before administering.
Urea (Urevert, Ureaphil) Dose: 1 g/kg	Give intravenously over 60 to 90 minutes. Use 30% solution (30 g/100 ml). Must be reconstituted. Onset in 30 to 40 minutes, peak in one hour, may persist for 5 to 6 hours. Unlike mannitol, urea crosses into the eye which may result in rebound increase in intraocular pressure after infusion is stopped. Do not use in patients with hepatic or renal dysfunction. Side effects include headache, nausea, vomiting, syncope, mental confusion, hypotension, and local reactions from mild to severe if solution extravasates.
Glycerin (Osmoglyn 50%, Glyrol 75%) Dose: 1 to 1.5 g/kg	For oral use. Generally use 4 to 8 ounces of the 50% solution and 3 to 5 ounces of the 75% solution. As effective as intravenous agents with only mild diuretic effect. Effective within one hour, duration of 4 to 5 hours. Metabolized to carbohydrates giving approximately 4.3 calories/g; thus, could be a problem in some diabetics. Chill before giving to improve palatability. Side effects are not common, but include headache, nausea, and vomiting.

lens stretches the iris snugly across its surface resulting in an increased pressure needed to force the aqueous humor through the iris-lens apposition. The resulting higher pressure behind the iris causes a slight bowing of the peripheral iris toward the trabecular meshwork. The extent of this forward movement depends on the rigidity of the peripheral iris. Even a small forward movement of the peripheral iris caused by slight pupil dilation will produce angle closure in individuals with a narrow angle formed by the iris and the cornea. In either situation, this anterior displacement of the peripheral iris causes it to isolate the trabecular network from the anterior chamber, thus preventing the outflow of aqueous humor. When the angle where the outer edge of the iris is attached to the cornea is completely closed, there is severe obstruction to outflow and the intraocular pressure can reach as high as 80 mmHg. When the canal of Schlemm is only partially blocked, the pressure will rise in proportion to the extent of closure. It is important to note that when the angle is open the pressure is normal.[4,8]

The lens itself continues to enlarge throughout life, pushing the iris forward. Due to the normal enlarging of the lens, patients over 50 years old with a shallow chamber are more prone to an attack than are younger patients. Patients predisposed to narrow-angle glaucoma also are usually far-sighted because the lens is often closer to the cornea than normal in hyperopic individuals. An attack of narrow-angle glaucoma in predisposed patients can be precipitated by pupil dilation caused by such factors as darkness, mydriatic drugs, or emotional stress.[1,8,9]

A special type of ophthalmoscope, known as a gonioscope, is used to detect the presence of a shallow anterior chamber. Because the pressure is normal when the angle is open, measuring the intraocular pressure will not detect the presence of a shallow chamber unless the patient is experiencing an attack at the time. Thus, routine tonometry is of minimal value in screening for patients predisposed to narrow-angle glaucoma.[10]

Narrow-angle glaucoma is characterized by intermittent attacks with spontaneous relief, or a sustained attack in which the pressure remains elevated. The symptoms of an intermittent attack include transient blurring of vision, halos around bright lights, pain in the eyes, and/or headaches. Pupillary constriction from light or sleep relieves the attack and the symptoms disappear. A sustained attack has the same onset as an intermittent attack, but the pupil does not constrict and the intraocular pressure continues to increase. As the pressure rises the symptoms become more severe with markedly blurred vision, pain, eye congestion, and often nausea and vomiting. Sustained narrow-angle attacks should be considered a medical emergency. Treatment is directed toward lowering the pressure to avoid permanent ocular damage.[4,8]

Following repeated intermittent attacks or a sustained attack of several days duration, adhesions of fibrous tissue may form between the iris and the corneal surface in the area of the trabecular network. These adhesions can permanently damage the trabecular network and lead to chronic secondary glaucoma even if the narrow-angle mechanism is corrected.[10]

The primary treatment of a sustained attack or prevention of future intermittent attacks is surgical. An iridectomy, using surgery or laser beam, provides an opening through the peripheral iris between the anterior and posterior chambers. This prevents the pressure in the posterior chamber from exceeding that of the anterior chamber.

Before surgery can be undertaken, the pressure must be brought under control. To accomplish this, hyperosmotic agents, such as mannitol, urea, or glycerin are used (Table 1). These agents create an osmotic gradient between the plasma and the anterior chamber causing fluid to be withdrawn and

thereby reduce the intraocular pressure.[11] Carbonic anhydrase inhibitors are used in conjunction with the hyperosmotic agents to reduce the formation of aqueous humor. Miotic drugs are used to constrict the pupil.[4,12]

Open-Angle Glaucoma

In open-angle glaucoma, the anatomy of the anterior chamber is not a factor. The increased pressure is the result of an unknown abnormality involving the trabecular network causing the interference in the outflow of aqueous humor to Schlemm's canal. This decrease in outflow occurs in the presence of a normal angle, thus the term "open-angle" glaucoma is used.[4,10]

While acute narrow-angle glaucoma is a medical emergency, chronic open-angle glaucoma is much more of a threat to vision because of its insidious onset. The intraocular pressure in open-angle glaucoma does not rise as fast or as high as in narrow-angle glaucoma. Thus, the disease is likely to be far advanced before the patient is aware of a loss of vision.[7]

The incidence of open-angle glaucoma increases with age and persons over 40 years of age should have intraocular pressure measured at least every 2 years. Open-angle glaucoma can be inherited and the offspring of a glaucoma patient should also have periodic pressure measurements on a yearly basis after age 40. Approximately 15 to 20% of the children of a patient with open-angle glaucoma will eventually develop increased intraocular pressure.[8] Open-angle glaucoma is also more prevalent among diabetics.[1,3]

Early open-angle glaucoma, being asymptomatic, is normally detected through routine screening of patients. Intraocular pressures above 20 mmHg are considered suspicious of glaucoma, and further evaluation of the eye is necessary. Pressures above 25 mmHg accompanied by optic disk changes and characteristic visual field changes, such as a decrease in peripheral vision, are indicative of glaucoma. Many practitioners presently feel that if the pressure is below 30 mmHg and the visual field and optic disk remain normal, the patient need not be treated for glaucoma because of the side effects and inconvenience of using eye drops. However, the patient should be followed closely for visual deterioration.[1,3]

The persistent elevation of pressure in uncontrolled open-angle glaucoma causes degeneration of the optic nerve. The degeneration results in a gradual, irreversible loss of peripheral vision and eventual blindness if the pressure is not reduced.[3]

Open-angle glaucoma is treated primarily with drugs. Surgery is reserved for the few cases that do not respond to maximal medical therapy. The agents utilized in controlling intraocular pressure are: (1) parasympathomimetic agents (cholinergic drugs and anticholinesterases); (2) sympathomimetic

Continued on Page 152

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WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCOCET®-5, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCOCET®-5 is subject to the Federal Controlled Substances Act.

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Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCOCET®-5 may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCOCET®-5 should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCOCET®-5 should not be administered to children.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions The administration of PERCOCET®-5 or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients PERCOCET®-5 should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. PERCOCET®-5 is given orally. The usual adult dose is one tablet every 6 hours as needed for pain.

DRUG INTERACTIONS The CNS depressant effects of PERCOCET®-5 may be additive with that of other CNS depressants. See WARNINGS.

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FOR MODERATE TO MODERATELY SEVERE PAIN

Acetaminophen with the narcotic difference

Reliable oral narcotic analgesia...

The narcotic component in PERCOCET®-5 is oxycodone, which is readily absorbed and provides dependable oral analgesia—usually within 15 to 30 minutes. Oxycodone can produce drug dependence of the morphine type and should be prescribed with the same degree of caution appropriate to the use of other narcotic-containing medications.

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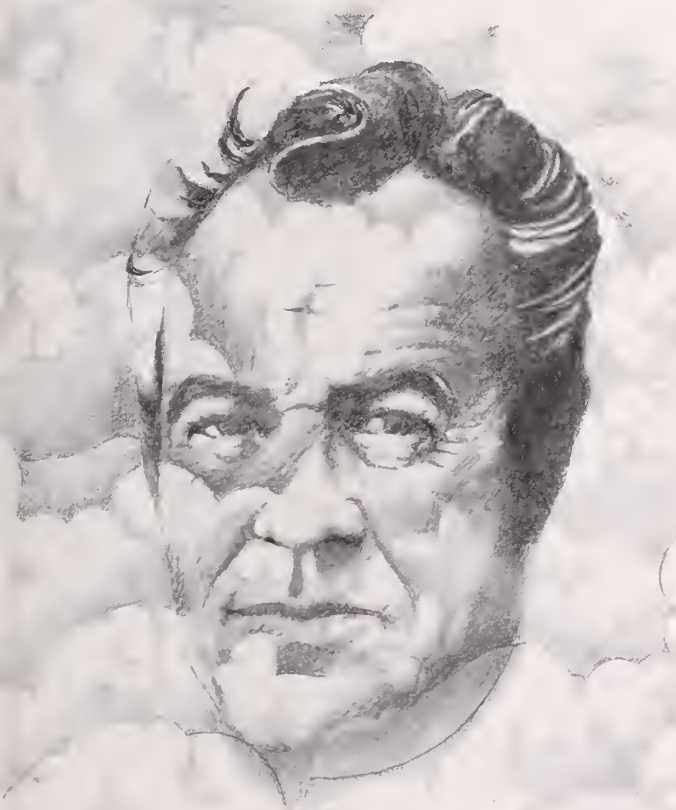
Acetaminophen is a non-narcotic analgesic widely used for aspirin-sensitive patients. Equivalent to aspirin in analgesia, it complements the pain relief provided by oxycodone.

The usual dose of PERCOCET®-5 is one tablet every six hours, providing convenience and economy for your patients. PERCOCET®-5 is ideally suited for your patients with aspirin sensitivity, with hemostatic disturbance, with peptic ulcer or on anticoagulation therapy.



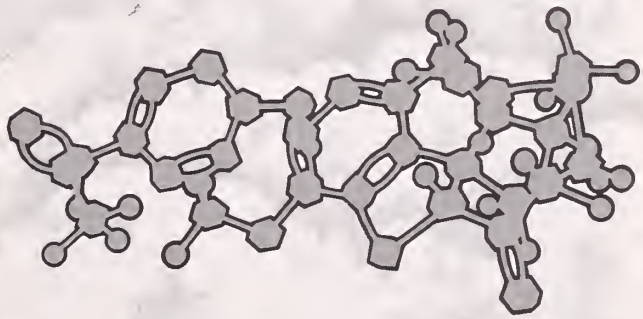
Tablets

Percocet®-5

each scored tablet contains 5 mg oxycodone HCl (WARNING: may be habit forming) and 325 mg acetaminophen

CII

When aspirin is contraindicated.



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agents, and (3) carbonic anhydrase inhibitors.

Drugs Used to Treat Glaucoma

Parasympathomimetic Agents

Stimulation of cholinergic receptors can be achieved by administration either of a cholinergic agonist or a cholinesterase inhibitor.

Cholinergic agonists. These are the most widely used parasympathomimetics used to treat open-angle glaucoma. Cholinergic agonists reduce intraocular pressure by facilitating the filtering of aqueous humor out of the anterior chamber through the trabecular network. They appear to dilate the trabecular network and veins leading away from Schlemm's canal, resulting in increased outflow. Contraction of the ciliary body caused by these drugs may also help open the trabecular network.[10,13]

Pilocarpine and carbachol are primary examples of cholinergic agonist drugs used in the treatment of open-angle glaucoma. Pilocarpine, the drug of choice in initial therapy, has an onset of action of approximately 15 minutes and a duration of about six hours.[12] Carbachol is more potent than pilocarpine, but has the disadvantage of poor corneal penetration. For this reason, carbachol is formulated with viscosity-increasing or wetting agents to enhance corneal permeability[10] (Table 2).

Side effects of cholinergic agents include local irritation, transient headaches, mild impairment of accommodation, and miosis. Night vision may be reduced by miosis and the patient should be warned about driving at night. Systemic reactions are rare and usually occur from overdosage.[12,13]

Treatment with pilocarpine is initiated with one or two drops of a 0.5 to 1% solution instilled up to every six hours. If this is not effective, the concentration is increased, up to 4%. There is usually no advantage of using strengths greater than 4%,[7,14,15] except in Negroes with heavily pigmented brown irides. The ocular pigmentation hinders the penetration of topically applied drugs to receptor sites and must be considered when adjusting the dose of pilocarpine in glaucomatous black patients.[16]

Concentrations above 4%, while not increasing the pressure-lowering effect, could prolong the duration of action and thereby permit twice-a-day dosing.[17] However, higher concentrations could also increase the likelihood of side effects.

A new method of pilocarpine administration is the Ocusert® system. It is a clear, flexible, elliptically-shaped object slightly larger than a contact lens. The unit is composed of two permeable membranes that surround the pilocarpine solution at the core. When the unit becomes wet in the eye, the drug diffuses out at a constant rate. The Ocusert is worn on the sclera underneath the upper or lower eyelid. The system is available as Pilo-20 or Pilo-40, and releases 20 and 40 μg of pilocarpine per hour, respectively. The majority of patients previously using 0.5% or 1% drops are controlled with Pilo-20; those using 2 to 4% drops require the Pilo-40. The unit is replaced by the patient every seven days. With this system much better control of intraocular pressure is obtained, especially during the early morning hours when diurnal variation usually results in a higher pressure. Furthermore, the likelihood of compliance is increased. However, the cost of the Ocusert system is approximately ten times that of eye drops.

Table 2

Parasympathomimetic Drugs Used in Glaucoma

Drug	*Usual Dose*
Cholinergic Agonists	
Pilocarpine	0.5 to 4% every 6 to 8 hours
Pilocarpine Ocusert	20 to 40 μg/hour, unit inserted weekly
Carbachol	0.75 to 3% every 6 to 8 hours
Cholinesterase Inhibitors	
Echothiophate iodide (Phospholine Iodide)	0.03 to 0.25% every 12 to 48 hours
Demecarium bromide (Humorsol)	0.125 to 0.25% every 12 to 48 hours
Isoflurophate (Floropryl)	0.01 to 0.1% every 12 to 72 hours

When the Ocusert is first inserted, there is an initial bolus of drug released that last about six to eight hours before the rate stabilizes. This initial release is approximately equal to one drop of 2% pilocarpine.

There have been no signs of ocular damage due to the Ocusert, but many patients experience irritation during the first few weeks of use. Another problem is the possibility of losing the Ocusert from the eye without realizing it. Considerable instruction is required during the initial period, but with continued use the patient becomes adjusted to wearing the unit and learns to sense its impending loss. The majority of patients prefer the Ocusert over drops, though some cannot adjust to the system and must return to drops.[18-21]

Carbachol is usually instilled two or three times a day in concentrations of 0.75 to 3%. Because of its poor corneal penetration, the response is often variable and may require more frequent administration. The primary indication for carbachol is in patients who are allergic to pilocarpine.[10,12]

Cholinesterase inhibitors. Drugs of this class act by inhibiting the enzyme acetylcholinesterase allowing the accumulation of acetylcholine at cholinergic receptor sites and a corresponding increase in parasympathetic activity. Thus, pressure is reduced because of an increase in aqueous outflow similar to that seen with cholinergic drugs, though the effects are more intense and longer lasting.[10]

Echothiophate iodide, demecarium bromide, and isoflurophate are all long-acting anticholinesterases and should not be used more than twice a day. Of these, echothiophate is the most frequently used; one drop is instilled into the eye every 12 to 48 hours in concentrations of 0.03 to 0.25%[13] (Table 2).

The anticholinesterase agents can induce the for-

mation of cataracts when used for extended periods or in maximal concentrations. Common local side effects are headache, ocular pain, blurring of vision, twitching of the eyelids, and congestion and spasm of the ciliary body.[10] Systemic side effects can occur following topical administration and include sweating, salivation, bradycardia, nausea, diarrhea, muscle weakness, and aggravation of bronchial asthma.[7] The long-lasting cholinesterase inhibitors should be discontinued at least three weeks prior to the use of succinylcholine, a neuromuscular blocking agent used in surgery that is metabolized by cholinesterase. Prolonged neuromuscular block or apnea have been reported in patients using echothiophate eye drops at the time of surgery.[22]

Because of side effects, the anticholinesterase agents are generally reserved for cases that do not respond to other drugs. Their tendency to produce cataracts and other adverse reactions can be minimized by employing the lowest effective concentration at the least frequent interval possible.[10]

Echothiophate must be reconstituted with the diluent provided before dispensing. The mixture is stable for approximately one month at room temperature or 12 months if kept refrigerated.

Sympathomimetic Drugs

Sympathomimetics increase aqueous outflow and decrease the rate of aqueous humor formation due to stimulation of alpha and beta adrenergic receptors. The mechanism is not fully understood. Epinephrine is the primary sympathomimetic utilized in open-angle glaucoma because it stimulates both alpha and beta receptors. Epinephrine is available as a borate, bitartrate, or hydrochloride salt and is used in strengths of 1 or 2% instilled every eight to 24 hours.[10,12]

Local reactions, such as burning, congestion, allergy and irritation, occur in approximately 25% of patients using epinephrine. Changing to another salt form will often reduce these side effects. The borate salt is thought to be better tolerated, but this is questionable.[7,14] Other side effects include headache, melanin deposition, and intermittent blurring of vision.[10] Epinephrine drops should be used cautiously in patients with cardiovascular disease because of systemic absorption. Digital pressure applied by the patient over the lacrimal sac located at the inner angle of the eyelids for two to three minutes minimizes systemic effects.[7]

The pressure-reducing effect of epinephrine is additive to that of other agents, and the drug is generally used in combination therapy. Epinephrine does not impair accommodation and is especially useful in counteracting the pupillary constriction produced by parasympathomimetic agents.[10]

Epinephrine solutions are unstable when exposed to light or the open atmosphere. The pharmacist should advise the patient regarding proper storage and the need for replacing the solution if it becomes discolored or turbid.

TABLE 3

CARBONIC ANHYDRASE INHIBITORS USED IN GLAUCOMA

Drug	*Usual Dose*
Acetazolamide (Diamox®)	250 mg 1 to 4 times daily, or 500 mg sustained-release capsule once or twice a day
Methazolamide (Neptazane)	50 to 100 mg every 6 hours
Dichlorphenamide (Oratrol)	50 mg every 6 hours
Ethoxzolamide (Cardrase)	125 mg every 6 hours

Carbonic Anhydrase Inhibitors

The carbonic anhydrase inhibitors are aromatic sulfonamides which, when given systemically, reduce the rate of aqueous humor formation by as much as 58%. The pressure-lowering effect is apparently due to a direct action on the ciliary body and is independent of the diuretic effect. The carbonic anhydrase inhibitors are not effective topically, nor do they lower the pressure in normotensive eyes.[12]

The agents available are acetazolamide, methazolamide, dichlorphenamide, and ethoxzolamide. Acetazolamide is most frequently used (see Table 3).

Side effects of carbonic anhydrase inhibitors are numerous and occasionally severe. Paresthesias of the face and extremities, drowsiness, fatigue, nausea, vomiting, diarrhea, and polydipsia are commonly observed; the majority of patients will experience at least some of these reactions.[12] Methazolamide appears to have a smaller incidence of calculus formation than acetazolamide.[23] Due to their metabolic effects on the kidney, carbonic anhydrase inhibitors can cause alkalinization of the urine which in theory could lead to an increased reabsorption of drugs such as quinidine, amphetamines, and tricyclic antidepressants.

Carbonic anhydrase inhibitors are added to the drug regimen in open-angle glaucoma when miotics and epinephrine are insufficient to control the pressure. Long-term use of carbonic anhydrase inhibitors is frequently unsuccessful due to the bothersome side effects, and they should be used with caution in patients who are sensitive to sulfonamides, who have severe kidney impairment, and who have renal calculi. In the emergency treatment of narrow-angle glaucoma, acetazolamide is often used intravenously in conjunction with hyperosmotic agents and miotics.[10]

THERAPEUTIC PLAN

The objective of treatment in open-angle glaucoma is to control the intraocular pressure, thus preventing visual field changes. Therapy is often initiated with pilocarpine, 2% up to four times a day; increasing to a 4% solution if necessary. Epinephrine, 2% twice a day, is added when pilocarpine alone is inadequate. If this combination will not control the pressure, because of tolerance or progression of the disease, carbonic anhydrase inhibitors can be added to the drug regimen. The an-

ticholinesterase agents are often reserved until last, because of their propensity to produce cataracts.[12]

Patients using a sympathomimetic and a miotic concurrently should be instructed to wait five to ten minutes between administration of the two drugs to allow the first to be absorbed through the cornea before instilling the second.[7] If anticholinesterase agents are needed, pilocarpine can be discontinued since there is no benefit from their simultaneous use.[24]

Potentially Hazardous Drugs in Patients With Glaucoma

The labeling of many drugs, such as anticholinergic agents or drugs with anticholinergic side effects, sympathomimetics, vasodilators, and steroids, state that they are contraindicated in glaucoma. This cautionary advice usually fails to recognize that glaucoma is not a single disease entity but consists of different types, i.e., narrow-angle and open-angle. Rarely will the warning specify in which type of glaucoma the drug is contraindicated. Drugs that may precipitate or adversely effect one type of glaucoma may have no influence or may even be beneficial in the other type.

Anticholinergic Drugs

Numerous drugs have anticholinergic activity including antihistamines, antiparkinson agents, gastrointestinal antispasmodics, preanesthetic agents, antipsychotic drugs, and antidepressants.[25] Many over-the-counter products, such as cold and allergy remedies and sleeping aids, also contain drugs with anticholinergic activity.

If a patient is predisposed to narrow-angle glaucoma, anticholinergics could precipitate an acute attack by dilating the pupil, thereby causing blockage of the trabecular network. When used to dilate the pupil during eye examinations, strong anticholinergics such as atropine, homatropine, cyclopentolate, and tropicamide have caused attacks of narrow-angle glaucoma. These agents should be avoided in patients with a shallow anterior chamber unless measures are available to control intraocular pressure.[26,27]

The systemic use of anticholinergic agents has at times been associated with narrow-angle attacks. This reaction is rare because the concentration of drug reaching the eye is usually not enough to produce sufficient dilation of the pupil for pupillary block. The risk depends on the ability of the drug to cause significant pupil dilation following systemic use. With strong anticholinergics such as atropine and scopolamine, there is a slight risk of precipitating an attack in predisposed patients while with weaker anticholinergics the risk is minimal.[27,28]

Patients with diagnosed narrow-angle glaucoma will most likely have had the ocular defect corrected surgically, or be under medical treatment, and would not be at risk after the use of systemic anticholinergics.[25] When attacks do occur following the use of systemic anticholinergics, it may not be certain that the drug was responsible since narrow-angle attacks can occur spontaneously in anatomically predisposed patients.[26]

In patients with open-angle glaucoma, anticholinergics could conceivably cause a worsening of the condition by relaxing the ciliary muscle, thus increasing the resistance to outflow of aqueous humor. In reality, this occurs rarely.[25,29] Patients with medically controlled open-angle glaucoma can be given systemic anticholinergic drugs without harmful ocular effects. The glaucoma medication will more than counteract any slight potential increase in intraocular pressure.[30,31] In addition, any unexpected rise in ocular pressure would be transient and the risk of further ocular damage is negligible.[27]

In patients with uncontrolled advanced open-angle glaucoma, the chronic systemic use of strong anticholinergics could be a potential problem. If potent anticholinergics must be used in these patients, the pressure should be monitored closely.[26]

Sympathomimetic Drugs

Sympathomimetic agents, such as vasoconstrictors, central nervous system stimulants, appetite depressants, and bronchodilators, have the ability to dilate the pupil. These agents are found in many prescription and over-the-counter products, and the accompanying labeling states that they are contraindicated in "glaucoma."

In patients predisposed to narrow-angle glaucoma, topical use of vasoconstrictors, found in many prescription and over-the-counter decongestant ophthalmic solutions, should be avoided. When used topically, these agents can cause sufficient pupil dilation to precipitate an attack. The systemic use of sympathomimetics in these individuals would present a slight risk of precipitating an attack because the concentration of drug reaching the eye might possibly be enough to produce pupillary block.[27]

In patients with open-angle glaucoma, the risk of topical or systemic sympathomimetic agents is negligible. Conversely, epinephrine, a sympathomimetic, is used to treat open-angle glaucoma. Yet the labeling of sympathomimetic drugs does not specify that they are contraindicated in narrow-angle glaucoma, but only in "glaucoma."

Vasodilators

The labeling of many systemic vasodilators states that they should be used with caution in glaucoma. This warning is based on the hypothesis that vasodilators may cause ciliary body vasodilation and an increase in aqueous humor production. Increased production could raise intraocular pressure. In reality, the ciliary vasodilation produced is relatively transient and no increase in pressure is apparent.[9] In patients with narrow-angle glaucoma, a relationship

Table 4

Estimate of Actual Risk Associated With Drugs "Contraindicated" in Glaucoma

I. Patients predisposed to narrow-angle glaucoma (less than 5% of glaucoma cases)

High Risk (Avoid)	*Slight Risk*	*Minimal Risk (in usual doses)*
Topical Anticholinergics	Oral Anticholinergics	Corticosteroids
Atropine	Atropine	Vasodilators
Homatropine	Scopolamine	Tricyclic antidepressants
Scopolamine	Belladonna	Phenothiazines
Cyclopentolate		Antihistamines
Tropicamide		
Topical Sympathomimetics	Oral Sympathomimetics	
Vasoconstrictors	Vasoconstrictors	
Naphozoline	Pseudoephedrine	
Tetrahydrozoline	Phenylephrine	
Epinephrine	Phenylpropanolamine	
Ephedrine	Ephedrine	
	Methoxyphenamine	
	Amphetamines	
	Appetite suppressants	
	Bronchodilators	
	Central nervous system stimulants	

II. Patients with controlled open-angle glaucoma (90% of glaucoma cases)

High Risk (Avoid)	*Slight Risk*	*Minimal Risk (in usual doses)*
None	Topical Steroids (especially potent agents)	Topical and Oral Anticholinergics
	Dexamethasone	Antihistamines
	Betamethasone	Tricyclic antidepressants
	Oral Corticosteroids	Phenothiazines
		Benzodiazepines
		Vasodilators
		Nitrites
		Nitrates
		Tolazoline
		Hydralazine
		Nylidrin
		Nicotinic acid
		Cyclandelate
		Isoxsuprine
		Papaverine

between vasodilators and precipitation of an attack has not been demonstrated.[27,31] In a study involving patients with very narrow angles, no attacks occurred after administration of vasodilators.[26]

The effect of vasodilators in open-angle glaucoma has also been studied. In a group of patients with open-angle glaucoma who were given oral vasodilators, no significant change in intraocular pressure was noted, even when their glaucoma medication was discontinued.[32] Another study detected no significant change in intraocular pressure when vasodilators were given intravenously to patients with open-angle glaucoma.[33] Thus systemic use of vasodilators carries little hazard in either narrow- or open-angle glaucoma.

Corticosteroids

Corticosteroids raise the intraocular pressure, possibly by increasing the resistance to outflow in the trabecular network. Steroids do not influence the pupil and, therefore, are not contraindicated in narrow-angle glaucoma.[24,27]

Topical administration of corticosteroids can significantly elevate intraocular pressure. With long-term therapy, this rise in pressure may induce secondary open-angle glaucoma.[28] The degree of pressure elevation is related to the anti-inflammatory potency of the steroid and the sensitivity of the patient. The more potent steroids, such as betamethasone and dexamethasone, tend to increase the pressure more than weaker agents, such as prednisolone and medrysone.[34,35] The frequency of administration and duration of therapy will also influence the degree of pressure increase. To minimize possible adverse effects of ocular steroid therapy, the least potent agent in the smallest effective dose should be used for as short a duration as possible.[35] Pharmacists should be cautious about refilling prescriptions for steroid eyedrops unless the prescriber is aware of the continuing use by the patient.

The risk of inducing glaucoma with systemic steroids is much less than the risk associated with topical administration. Although systemic steroids can increase intraocular pressure, this occurs infrequently, but the response again depends on the sensitivity of the patient.[26] In patients with existing open-angle glaucoma, there have been reports of

systemic steroids aggravating the condition. However, providing the intraocular pressure is monitored, systemic steroids can be safely used in these patients.[26,31]

Conclusion

There is no definite contraindication to the use of systemic medications in patients with controlled open-angle glaucoma. In the rare patient predisposed to narrow-angle glaucoma, some topical and systemic medications may carry a risk (Table 4). If the patient is known to be predisposed to narrow-angle glaucoma, the condition will most likely have been corrected surgically and there would be no risk in using these drugs.

Pharmacist's Role in Glaucoma

The pharmacist can help in screening for individuals predisposed to narrow-angle glaucoma by questioning patients when they request over-the-counter eyedrops. The following points may indicate that the patient needs to be evaluated for the presence of a narrow-angle:

(1) Eyedrops requested for ocular pain associated with headache, blurring of vision, redness of the eyes, and rainbow halos around lights. Patients may associate these symptoms with "tired eyes." Nausea, vomiting and sweating can also occur.

(2) Upon questioning, patient admits to ocular discomfort in the evening, when watching television, or a movie in a darkened room or during periods of anxiety.

(3) Attacks of ocular discomfort are self-limiting, especially when the patient is exposed to light. For example, the patient may have ocular pain while watching television, but the symptoms are relieved upon entering a well-lighted room. The ocular discomfort will probably have subsided by the time the patient comes to the pharmacist, but a product for future use may be requested.

In conjunction with the above symptoms, the following factors indicate an increased susceptibility to narrow-angle glaucoma attacks: a family history of narrow-angle glaucoma, age over 50 years, farsightedness, or current therapy with a medication that might have a slight chance of precipitating an attack.

If symptoms are severe, the patient should be advised to seek medical attention immediately.

The pharmacist can assist patients in the treatment of open-angle glaucoma by:

(1) Advising the patient on the proper method of administering eyedrops.

(2) Monitoring refill frequency to check for compliance.

(3) Emphasizing to the patient the importance of compliance. This is especially important in a disease such as open-angle glaucoma where there usually are no symptoms.

(4) Keeping records up to date on dosage adjustments by the physician.

(5) Questioning the patient about side effects. If severe, suggest contacting the physician. If therapy has just been initiated, explain to the patient that the side effect may become less bothersome in several weeks.

(6) Explaining the decrease in night vision if the patient is using a miotic and warning about driving at night.

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DATA PATTERNS SHOW GREAT VARIATIONS

Maine is in the advantageous position of having collected several years of data on 100% of patients discharged from acute hospitals. The combining of this data with census data has developed a capability to perform population based analysis of Maine's health care use patterns.

Use patterns that do not contain identifiers are considered to be non-confidential and as such may be disseminated freely. The Maine Health Data Service staff, who maintain the State file, have performed extensive analysis in responding to requests for special studies. This analysis has produced a variety of use patterns that are felt to be of general interest. The remainder of this article will attempt to familiarize the reader with the type of information that can be produced from the Statewide file.

The seasonal variations in use of acute care hospitals by Maine residents was selected as being of general interest.

Maine Residents

One hundred sixty-seven thousand, seven hundred and seventy-three Maine residents (newborns not included) used 1,147,441 hospital days in 1975.

The average length of stay was 6.84 days — the average daily census was 3,144.

Monthly Ranking by Average Daily Census

1) 3,449 — January
2) 3,348 — February
3) 3,230 — March
4) 3,212 — September
5) 3,182 — April
6) 3,175 — October
7) 3,153 — June
8) 3,089 — May
9) 3,028 — November
10) 2,980 — July
11) 2,965 — August
12) 2,932 — December

In January 14,429 Maine residents used 106,931 days with a LOS of 7.16 compared to December when 13,193 Maine residents used 90,896 days with a LOS of 6.89.

The additional 1,736 patients represent a change of 12.16%.

The additional 16,035 days represent a change of 17.63%.

The degree of change in use of acute care facilities during each of these months may more easily be understood by using an estimated dollar value. Applying the current daily Blue Cross per diem of $230 to the 16,035 days would indicate that there would have been over 3½ million dollars less billings in December than in January.

Those planning for change in Maine's health care system enjoy a tremendous advantage over their counterparts in most of the other states in the union in being able to have ready access to the kinds of data outlined in this article. Physicians or others wanting information from the 100% discharge data file should contact John Putnam, Maine Health Data Service, 110 Free Street, Portland, Maine, 04101 (775-3536).

Necrologies

John F. Dougherty, M.D.

1906-1978

Dr. Dougherty

Dr. John F. Dougherty, 71, of Bath, Maine, President of the Maine Medical Association from 1965-1966, died on March 6 following a long illness.

Born in Bath, on November 27, 1906, he was the son of Daniel T. and Catherine G. Dougherty.

He attended Georgetown University, the University of Maine and Bates College and received his medical degree from Boston University School of Medicine in 1939. He served in the U.S. Army Medical Corps as a Major from 1941 to 1946. In 1946, he located in Bath and was a member of the staff at the Bath Memorial Hospital from 1946 to 1976 and served as chief of obstetrics from 1954 to 1964. He retired in March 1976, but continued to serve as physician advisor until he became ill last October.

Dr. Dougherty was a senior member of the Lincoln-Sagadahoc County Medical Society and the Maine Medical Association. He was Councilor for the Third District of the M.M.A. from 1959 to 1965, serving as Council Chairman in 1963-1964, President elect in 1964-1965 and President in 1965-1966. He was also staff secretary at the Bath Memorial Hospital from 1957 to 1972 and vice president of the staff from 1973 to 1975.

Surviving are his widow, Esther Drummond Hawley Dougherty, and several cousins.

Harlow B. Rowell, M.D.

1909-1978

Dr. Harlow B. Rowell, 69, of York, Maine, died on March 11 at a local hospital following a short illness.

He was born in Hales Bar, Tennessee on January 23, 1909, son of George F. and Florence H. Rowell.

Dr. Rowell was graduated from Haverford College in Pennsylvania, received his medical degree from the University of Pennsylvania School of Medicine in 1934 and interned at the Philadelphia General Hospital.

Prior to establishing a practice in Wallington, Pennsylvania, he served as a physician at the Pennsylvania Eastern Penitentiary in Philadelphia. In 1976, he located in York and was affiliated at the York Hospital's Emergency Room Department.

He was a member of the York County Medical Society and the Maine Medical Association.

Surviving are his widow, Dorothy Clark Rowell of York Beach; two brothers, George F. Rowell of Florida and Edward S. Rowell of Wellsboro, Pennsylvania; and a sister, Mrs. Marion R. Linton of Wellsboro, Pennsylvania.

Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The Maine Medical Association's House of Delegates, at its June 1976 meeting, adopted a regulation stating that a *minimum of 150* hours of continuing medical education is required in order to maintain membership. The policy took effect on January 1, 1977 and all members must be certified by January 1, 1980. Eligibility for certification begins January 1, 1977.

Credits required for the three-year period are as follows:

Category 1 — CME Activities with Accredited Sponsorship **(60 hours required)**	**No limit**
Category 2 — CME Activities with Non-accredited Sponsorship	**45 hours**
Category 3 — Medical Teaching	**45 hours**
Category 4 — Papers, Publications, Book and Exhibits	**40 hours**
Category 5 — Non-supervised individual CME Activities	**45 hours**
Category 6 — Other Meritorious Learning Experience	**45 hours**

Only active, dues-paying members are required to report. Please fill in your activity report promptly and return to the M.M.A. office, P. O. Box 250, Brunswick, Maine 04011.

County Society Notes

Continued from Page 111

A report of the House of Delegates meeting, which was held December 10, 1977, at the Mid-Maine Medical Center in Waterville was given by Dr. Maurice Ross, our member to the Executive Committee of the Maine Medical Association. He discussed the report of Dr. Hill, President of this group, concerning the status of the "Medicaid Cutback" and other legal and legislative matters. He also mentioned "Health Care Financing," "Building," "Malpractice," "Committee Reports," etc.

Correspondence: Letter from Dr. English and Dr. Hazzard, concerning a combined meeting of the members of the Maine Bar Association, Maine Medical Association, Osteopathic Association from York, Sagadahoc, Oxford, Androscoggin and Cumberland Counties.

The tentative date is February 16, 1978 at the Red Coach Grill, Portland, Maine.

Letter from Assistant Director, Mr. D. Jeffrey Hollingsworth regarding the outcome of "Certificate of Need" session on November 15, 1977 in Augusta.

Letter about Guidelines for Health Planning of which all members, I believe, received a copy.

Letter from Assistant Executive Director concerning items suggested by Dr. Bacon. Apropos to this, Dr. Ross stated the merits to being a member of the Maine Medical Association which includes the York County Medical Society.

There were twenty physicians and three guests present.

The meeting was adjourned at 9:30 p.m.

MELVIN BACON, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association met at Guido's Wine Cellar in Augusta, Maine on February 16, 1978, with 63 members and guests in attendance. Following a most delicious repast, the meeting was called to order by our President, Dr. Richard E. Barron at 8:30 p.m.

Correspondence: Correspondence concerning an audit clinic was passed out to the members.

There was no new business.

Old Business: The nominating committee recommended the name of Dr. O. Thomas Feagin for nomination to the Executive Committee of the Maine Medical Association and the members voted to cast a single ballot for this nomination.

The program consisted of a presentation by Miss Laura Franciose of the Maine Blue Cross and Blue Shield on the subject of cost containment in the hospital. A film entitled, "The Buck Starts Here" was shown and there was an exchange of ideas among the members present and the Blue Cross representatives concerning the various ways and means in which physicians could be involved in the control of costs to the patients.

Meeting was adjourned at 9:30 p.m.

O. THOMAS FEAGIN, M.D., *Secretary*

Penobscot

The February meeting of the Penobscot County Medical Society was held on February 21, 1978 at the Mary Jane Restaurant in Bangor.

In President Philip G. Hunter's absence, the meeting was opened by Secretary Jurgeleit and the minutes of the January meeting were approved. Announcement was made of the Audit Clinic sponsored by the JCAH and the Maine Hospital Association Research and Education Trust that is to be held in Augusta in March. It was noted that the Department of Human Services plans to revise the current Medicaid fee schedule and is asking for physician input; specialty societies, in particular, have been asked to make suggestions in regard to the fee schedule. Dr. Francis I. Kittredge emphasized that such physician input into this fee schedule is essential.

The application for membership of Dr. Jordan Shubert was presented and unanimously approved.

Mr. D. Jeffrey Hollingsworth, the Assistant Executive Director of the Maine Medical Association, then presented a summary of some of the current proceedings in the Maine Legislature as related to health care. In particular, he noted the considerable debate and lobbying that took place regarding the certificate of need bill. There followed a lengthy question, comment, and discussion session regarding the physician's role in the political process. It was emphasized by both Drs. George W. Wood, III and Charles D. McEvoy, Jr., that we, as physicians, are going to have to communicate more on a personal basis with our legislators to try to counteract the general feeling of antagonism toward the medical profession that seems to exist in the political sphere today.

There being no further business, the meeting was adjourned at 10:15 p.m.

H. CLEMENT JURGELEIT, M.D., *Secretary*

Franklin

A meeting of the Franklin County Medical Society was held on March 6, 1978.

The meeting was called to order by the President, Dr. James R. MacMahon.

1. President MacMahon introduced guest speakers Drs. Jeremy Morton, William Medd and Mr. John Schroeder who spoke on the malpractice insurance company being formed in the State by physicians.

2. Following the presentation and discussion of this issue, the County Society discussed the request for physician representation to a civil defense disaster planning session to be held March 16 at the Community Center. Dr. Dale D. Bardo, head of the Franklin County Memorial Hospital Emergency Room, was volunteered and was nominated to represent the County Society at that planning session.

3. A presentation regarding the AMA negotiation seminar was made. Leaflets describing this were sent to the medical staff of the Franklin County Memorial Hospital with the suggestion that members of the Executive Committee might wish to attend. The upcoming Medicare reimbursement list publications were discussed and suggestions made via the AMA literature were mold. The County Society decided to take no preemptive action pending actual publication.

4. Dr. MacMahon announced that there would be an upcoming medical-legal panel to be held in Waterville sometime in the month of March. He would announce to the membership when a specific date, time and place have been set.

DANIEL K. ONION, M.D., *Secretary*

Androscoggin

The March meeting of the Androscoggin County Medical Society was called to order by the Vice President, Dr. Lawrence A. Nadeau, at 8:00 p.m., following a social hour and dinner at No Tomatoes in Auburn on March 16, 1978, with 64 members present and 4 guests.

The secretary's report was accepted as read.

Correspondence included note of thanks from Dr. Ralph Zanca, request for change of classification from Dr. Helene M. Reeves and a communication from Mr. Cohen.

The request from Dr. Helene M. Reeves to change her membership classification from active to affiliate was approved and unanimously granted.

The Treasurer's Report and the Auditor's Report were read by Dr. Kenneth P. Wolf and placed on file.

Dr. Michael J. Harkins reported for the Finance Committee. A motion made and duly seconded was voted to give the Finance Committee a free hand in taking care of investments. Voted 60 to 5.

A motion by Dr. Stanley D. Rosenblatt and seconded by Dr. Paul M. Beegel to invite Mr. Cohen to speak at a future meeting

was carried. It was further moved by Dr. Leo E. Cousineau and seconded by Dr. Behzad Fakhery to leave the time to invite Mr. Cohen to the Executive Committee members.

A motion was made by Dr. Charles A. Hannigan to invite Mr. Hathaway to a future meeting. Following discussion and comments by Dr. Norman O. Gauvreau, the motion was defeated, 9 for, 20 against, 36 not voting.

The business meeting was adjourned for the program at 8:40 p.m.

Dr. Lawrence A. Nadeau introduced Dr. Douglas R. Hill, President of the Maine Medical Association, who extended appropriate greetings.

Speakers of the evening were Dr. Patrick Dowling, chairman of the Ad Hoc Committee on Malpractice of the M.M.A., Dr. William Maxwell, President of Mutual Physicians' Insurance Co. of Maine, Mr. John Schroeder, Vice-President of Johnson and Higgins, an Insurance Brokerage Firm. A most informative program was presented on the organization of the Physicians' Mutual Insurance Co. of Maine, their need and their plans for the future. It is planned to start signing up members by July 1st, pending Insurance Commission approval. There are 1,230 physicians and they need 500 to start functioning. There were several graphic charts to supplement their talk. The conference was followed with discussion by members of the Society.

The meeting adjourned at 10:15 p.m.

KENNETH P. WOLF, M.D., *Secretary*

Letters to the Editor

To the Editor:

Re: Coma and Cimetadine Therapy

A recent correspondence in the February 2, 1978 issue of the *New England Journal of Medicine* and another in the *Lancet* have directed attention to the uncommon occurrence of mental confusion in coma with cimetadine therapy. I think it timely to report a similar incident occurring at the Maine Medical Center.

The patient is a 70-year-old female with a 50 pack/year history of cigarette use, admitted on January 27, 1978, for an acute exacerbation of her pulmonary disease. Initial treatment with bronchodilators, intravenous solu-medrol and ampicillin did not prevent the gradual respiratory failure which necessitated assisted ventilation on January 31st. On February 1st, she was begun on cimetadine 300 mgs IV q6h, when her nasogastric aspirate tested positive for occult blood. Her pulmonary status gradually improved enough to allow extubation on February 4th, only requiring reintubation on February 8th when her pulmonary function again deteriorated. At this point, a melanotic stool and fresh bleeding on gastric lavage were noted, treated with continued cimetadine and temporarily with pitressin .3 units per IV drip. Transfusions stabilized her hematocrit in the 35-40% range, at which time endoscopy revealed numerous superficial gastric erosions without ulcer craters or varicies.

On February 12th, the patient was begun on total parenteral nutrition via the left subclavian vein.

On the morning of February 14th, the patient, at all times previously easily arousable, was noted to be completely unresponsive to deep painful stimuli. No focal neurological signs were present. A lumbar puncture was normal, arterial blood gases on 30-40% O_2 for day were pH 7.41 to 7.48, PCO_2 52-84, PO_2 61-82.

Serum ammonia was 64, blood glucoses 180-283, magnesium 2.9, calcium 7.4 with albumin 2.4 (unchanged from admission), hematocrit 32, sodium 147, potassium 4.1, chloride 83, CO_2 52 (chronic metabolic alkalosis). On February 15th, at 2:00 P.M., the patient continued to be completely unresponsive, her cimetadine was discontinued as a possible contributing cause, all other medications and her TPN were continued unchanged. When seen by her physicians on the following morning, she was again able to open her eyes on verbal command and able to answer questions by nodding her head. She remained alert throughout the day; however, during the night of February 16th, she again became obtunded and on the morning of February 17th was noted to be stuporous, responding to painful stimuli only with withdrawal of her extremities and some grimacing movements. However, later on the morning of February 17th she was again noted to open her eyes on verbal stimuli, and could again answer questions by nodding her head. She has remained arousable over the following six days.

Although this patient has multiple problems, and cimetadine can not with certainty be incriminated as a cause of her coma, I believe the discontinuation of cimetadine and the improvement in her mental status are more than coincidentally related.

JOHN T. DEVLIN, M.D.
Medical Resident
Maine Medical Center
Portland, Maine 04102

To the Editor:

As part of the Office of Professional Programs effort to keep health professionals informed about newly approved drugs, we will send a copy of the "Summary for Basis of Approval," for Sodium Valporate, the new Antiepileptic Drug, to interested physicians.

We would appreciate it if you will carry an announcement of this in *The Journal of the Maine Medical Association*. If you do, would you please ask your readers to enclose a self-addressed label when they write for a copy.

After reviewing this document, if the physician has any comments on its usefulness, or suggestions for improvement, we would appreciate hearing about them.

ALAN S. KAPLAN, M.D., M.P.H.
Director, Professional Programs
Dept. of Health, Education, and Welfare
Public Health Service
Food and Drug Administration
Rockville, Maryland 20857

Mailgram to the Editor:

Today, April 7, 1978, United States District Court for the District of Columbia issued an order which enjoins, pending further proceedings, the MAC's for Chlordiazepoxide HCl which had been scheduled to take effect Monday, April 10, 1978. This means there is no federal MAC now in effect for Chlordiazepoxide HCl and there will not be, at least until further court proceedings.

Health Care & Business Planning Dept.
Roche Laboratories

DRUG THERAPY REVIEWS — Drug Therapy of Glaucoma — Continued from Page 156

sure in patients with glaucoma. Curr Ther Res 17: 156-160, (Feb) 1975.
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34. Podos, S. M., Krupen, T., Asseff, C., et al: Topically administered corticosteroid preparations — comparisons of intraocular pressure effects. Arch Ophthalmol 86: 251-254, (Sep) 1971.
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The Journal of the Maine Medical Association

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Oral Contraceptive Therapy and Benign Hepatic Lesions in Females

JOHN ZERNER, M.D., F.A.C.O.G.*, JOSEPH L. WILKIS, M.D., F.A.C.O.G.** and MARY ELLEN FENN, M.D., F.A.C.O.G.***

Articles have suggested an association between the finding of benign hepatic lesions in women and the use of oral contraceptive agents. Recently three females presented with abnormalities of this sort. The first patient, however, had essentially no exposure to exogenous hormonal therapy. The second and third has used oral contraceptives, but in the distant past. Because of these findings we feel it is important to record these cases and to review the literature briefly.

CASE REPORTS

Case #1. S. M., a 32-year-old, white, married Gravida 11, Para 11 was admitted to MMC on 2/1/77 with diagnosis of teratoma of the right ovary. She also requested sterilization. The first diagnosis had been made on the basis of x-ray findings showing a tooth-like structure present in the right adnexal area. Past history elicited the fact that the patient had been on oral contraceptives (Ethinyl Etradiol 0.05 mg. and Norgestrol 0.5 mg.) for a period of but two weeks (1972), discontinuing same because of personal preferences. The patient had used an IUD both before and after this episode for contraception. No history of any hepatic disease was elicited. Family history was also negative for malignancy.

After preoperative evaluation was completed and considered normal, on 1/10/77 examination under anesthesia, fractional curettage, and exploratory laparotomy were performed. As expected, the right ovary was distorted by an adult cystic teratoma. The remainder of pelvic findings were normal. Exploration of the upper abdomen, however, revealed a 5 cm. x 6 cm. hepatic mass in the area of the gallbladder itself. The pelvic surgery was completed performing: 1). right salpingo-oophorectomy, 2) wedge resection of the left ovary, and 3) left fimbriectomy. Frozen section of the right ovarian lesion revealed adult cystic teratoma. The first incision was closed; a right subcostal incision was then made to expose the hepatic area. Two distinct and separate nodules were noted near the gallbladder with the first essentially distorting the gallbladder itself. A partial hepatectomy and cholecystectomy were performed. Frozen section of the lesions revealed focal nodular hyperplasia of the liver.

The patient's postoperative course was unremarkable and discharge occurred on the 5th postop day.

Final pathological report: 1. Focal nodular hyperplasia of the liver with free margins, and 2. Adult cystic teratoma, right ovary.

To the present, physical examination, liver enzyme studies, and a liver scan (1/4/78) have been considered within normal limits.

Case #2. C. D., a 21-year-old, white, single Gravida 0, Para 0, whose LMP was 3/1/76 admitted to MMC with a 48-hour history of right upper quadrant pain with radiation to the back. The patient had previously been admitted 2/76 with history of epigastric pain. Evaluation at that time, including upper G.I. series, oral cholecystogram and SMA 12/60 were within normal limits. CBC was normal but sed rate was reported as 30. Pelvic examination at initial admission gave evidence of bilateral salpingitis (the patient having previous history of pelvic inflammatory disease and positive GC culture obtained). Impression at the first admission was Curtis Fitz-Hugh syndrome. The patient was discharged on Ampicillin.

This patient had been on Norethindrone 1 mg. and Mestranol 0.05 mg. for contraception in the years 1972 to 1973. She had used foam, condoms, and diaphragms since that time. The patient on readmission (3/76) complained of continual right upper quadrant pain. On examination the liver was enlarged and distorted by a mass extending eight centimeters below the right costovertebral margin. Repeat oral cholecystrogram was performed and considered normal, but a liver scan showed abnormalities to be present. As the patient's hematocrit dropped significantly, intraabdominal bleeding was suspected and she was taken to the Operating Room on 3/10/76 for exploration. On entering the abdomen a intrahepatic hematoma was noted involving the inferior aspects of the right lobe and the midline segment of the left lobe. The hematoma was evacuated and biopsies of the hematoma wall were obtained. Postoperative course was benign and she was discharged to be followed in her physician's office.

Pathology report showed only intrahepatic organizing hematoma with normal hepatic tissue present at the periphery. There was no evidence of any malignancy.

For reprints, write 260 Western Ave., South Portland, Maine 04106.

*Active Medical Staff, Mercy Hospital, Portland, Maine 04101.

**Courtesy Medical Staff, Mercy Hospital, Portland, Maine 04101.

***Courtesy Medical Staff, Mercy Hospital, Portland, Maine 04101.

Case #3. E. S., a 35-year-old white, married Gravida 11, Para 11 was admitted for total abdominal hysterectomy. The patient had had an abnormal Pap smear. Colposcopic evaluation with directed biopsies showed there to be carcinoma in situ of the cervix (CIN-111) with negative endocervical curettings. This patient had used Norethynodrel 2.5 mgs. and Mestranol 0.1 mg. for contraception in the years 1968-1971. From 1971 to 1973, a Safe-T-Coil was used for contraception and in 1973 this was removed with CU7 being inserted.

The patient was taken to the Operating Room where a lower abdominal incision was made. Exploration of the abdominal contents revealed nodules to be present in the liver. Surgical consultation was obtained and, under direct visualization, biopsies of these lesions were taken.

Pathology report showed focal nodular hyperplasia. The patient then underwent total abdominal hysterectomy and resection of the hepatic lesions. Postoperative course was benign and she is being followed through her physician's office.

Final pathology report showed: 1. Focal nodular hyperplasia of liver, and 2. Severe dysplasia of the cervix.

First reported by Baum[3] in 1973, the appearance of benign liver lesions in females using oral contraception has been steadily increasing over the past years. To date, over 200 patients have been discovered. The greatest number have been found to have one of two lesions: focal nodular hyperplasia (FNH) or hepatic adenomas (HA).

Confusion exists in the definition of many terms that are used for these two benign lesions.[13,17] "FNH" has been called adenoma, benign hepatoma, focal cirrhosis, hematomatous cholangiohepatoma, hepatoma, mixed adenoma, solitary hyperplastic nodule, and isolated nodule of regenerative hyperplasia.[12] HA conversely is known as benign hepatoma and hepatic solitary adenoma. Nissen[23] describes the situation as "a somatic nightmare" as few institutions have had a large enough experience in diagnosing this lesion. Edmunson points out that the absence of histologic criteria has resulted in error and confusion.[8] The term benign hepatoma should be avoided as the term hepatoma in itself implies hepatocellular carcinoma.[13]

Hence, two descriptive phrases are to be encouraged in the case of benign hepatic lesions: focal nodular hyperplasia (FNH) and hepatic cell adenoma (HA). The former occurs more often than the latter in a ratio of 3:1. Both are benign[1] with no evidence of malignant transformation.[12] The greatest majority of these tumors occur in the reproductive period of life with the average age being under 35 years.[19] The right side of the liver is more commonly involved.[15]

Microscopically FNH and HA are distinguishable with careful observation.[17] FNH has no capsule but may be well demarcated with central scarring, nodular parenchyma, bile ductules and large veins and arteries at the periphery and in some septa. HA may have partial or complete capsulization, but no central scarring or parenchymal nodularity. HA is also without bile ducts, ductules or peripheral vascularity. However, it is to be remembered in the face of

Continued on Page 163

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***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy. Advise patients to discuss therapy if they intend to or do become pregnant.**

As with all anticholinergics, inhibition of lactation may occur

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established.

Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated, avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment, blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets

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hemorrhage, the original pathology may be obscured.[13]

Initial presentation of the patient with these lesions may vary. Acutely, the patient may suddenly develop symptoms of acute cholecystitis.[2,6] Further hemoperitoneum and shock,[5,7] secondary to rupture of the hepatic lesions,[2,17,14] may occur. Interestingly, the rupture is often associated with the onset of menstruation.[9] This may be related to the constriction of the arteries supplying the lesion, in a way similar to the spasm occurring in the spiral arterioles of the endometrium at the time of menses. Alternatively, symptoms may be gradual[1] with right upper quadrant discomfort slowly increasing in intensity followed by the discovery of a mass in this area.[5,9,11,19] Finally, the patient may be asymptomatic with the lesion being discovered by palpation of a mass in the right upper quadrant[12,9,10] or at the time of surgery performed for other reasons, usually hysterectomy or tubal ligation.[11] This is the manner of discovery in 10% of the reported cases.[13]

Diagnosis is difficult[2] although one should suspect lesions of this sort in any young female who has been on oral contraceptives and now complains of right upper quadrant discomfort or in whom a right upper quadrant mass is palpated. Routine laboratory studies are not useful.[14,24]

Liver scan, when the lesions are large enough, may be helpful, both preoperatively and for follow-up evaluation.[1,5,19] Sonography is useful to evaluate a hepatic mass and to distinguish a solid from fluid filled tumor, but a negative result does not rule out either HA or FNH. Angiography has been used[1,13,24] as has been computerized axial tomography ("CAT Scan"). However, the latter is prohibitively expensive, but for a few institutions.[13] Percutaneous needle biopsies are to be avoided because of the vascular nature of the lesion.[2]

Treatment optimally starts with a meticulous evaluation at the time of surgery. The location of the lesion, observing whether the lesion is multi-or unifocal, and ascertaining the tumor type are three basic considerations. Removal of the lesion whenever possible,[2] either with lobectomy or partial hepatectomy, is encouraged.[5] Yet this is not always possible, especially in the face of shock secondary to hepatic rupture and bleeding. Here the proper course after biopsying may be ligation of the hepatic artery supplying the lobe harboring the tumor and in so doing hemostasis and blood volume replacement can be achieved. Definitive therapy in this situation can be carried out electively at a later date. This is especially true if the physician involved is not conversant with hepatic anatomy. Discontinuing the use of oral contraceptives is obvious.[5]

An anectodal case involving biopsy alone in a patient having focal nodular hyperplasia was reported.[13] No excision could be performed as the patient was in marked shock and the lesion could not be removed. Discontinuance of oral contraceptives resulted in the lesion essentially disappearing. Therefore, it may be a suggestion that focal nodular hyperplasia could well be left in place once the diagnosis has been made; however, this mode of therapy will require further researching before its advocacy can be advised.

Etiology is open to much discussion. Prior to the use of oral contraception, few cases of either FNH or HA were reported.[1,12] However, since their introduction, numerous reports have confirmed a rapid increase in the number of these lesions.[4,5] Kent[13] reports 78 patients in whom benign lesions were found and of these, over 85% had been on oral contraceptives for more than four years and over 50% for more than five years; 13.5%, however, had less than two years of exposure. Duration of exposure therefore is most significant in the development of these lesions and is confirmed by others with the relative risk increasing dramatically after 60 months of continuous usage.[9,21]

It behooves us to look closer at the components of the oral contraceptives themselves. The liver is very sensitive to both estrogenic and progestational compounds.[10,11] Synthetic estrogens are Mestranol and Ethinyl Estradiol. To date Mestranol has been implicated in the greater number of cases; however, this incidence may be a reflection of the compounds wider and longer availability.[18] Interestingly, Mestranol is first demethylated to Ethinyl Estradiol by the liver. Both estrogenic compounds are associated with cholestasis,[16] diminishing the ability of the liver to clear conjugated toxic metabolites. Also they act directly upon the hepatic vascular system producing: 1) loss of arterial elasticity, and 2) thickening of the venous wall. These may lead to hypoxia of the hepatocytes with resultant proliferation as a form of hepatic adaption to stress as is seen in both FNH and HA.

Like estrogens, progestional compounds may alter the hepatic enzyme system, leading to cholestasis and the decreased clearing of metabolites. Further, some of the progestins have a close structural relationship with certain androgenic compounds used in anabolic steriod therapy which in themselves have been associated with development of hepatocellular carcinoma.[2,15,16] Norethynodrel experimentally has also caused hepatic tumor in animals.[9] All in all, however, the progestins do not appear as important as the synthetic estrogens in producing liver alterations.[9]

Further evidence of hormonal influence is obtained in two recent articles. Ross[22] described a patient who had been found to have focal nodular hyperplasia at the time of exploratory laporotomy and whose lesion could not be resected completely. A postoperative hepatic angiogram showed the lesion to be present on the right side of the liver. Oral contraceptives were discontinued in August of 1974. Repeat liver scans in 1975 and 1976 showed regression of the lesion's size. The second patient, that of Mays and Christopher[15] had been on oral contraceptives for five years and was then found to have a liver

lesion and underwent a right lobectomy for "ruptured liver tumor." Pathology report showed focal nodular hyperplasia. The remainder of the liver was normal. The patient continued on oral contraceptives as at that point there had been no suggestion of the potential association of oral contraceptives and liver tumors. Six years later the patient underwent a second exploration for a hepatic mass and was found to have a similar and separate lesion present.

Quite frankly, however, the absolute correlation of oral contraceptives and the development of hepatic tumors has not been established. One patient in our series (Case #1) had been on oral contraceptives for less than two weeks. Indeed, O'Sullivan[20] mentioned a 19-year-old Gravida 0, Para 0, who, at the time of cholecystectomy, was found to have focal nodular hyperplasia. No evidence of oral contraceptive usage was ever elicited in spite of exhaustive inquiries.

In summary then, it is strongly advocated that all women presently on oral contraceptives have as part of their physical exams, careful palpation of the hepatic area.[1,9] Further, should any woman on oral contraceptives complain of progressive or sudden right upper quadrant discomfort, the diagnosis of benign hepatic tumor must be entertained.[6,9]

All cases of this type should be reported and reviewed by the liver tumor registeries now being established in the United States.

Acknowledgements

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Cervical Carcinoma During Pregnancy

CHARLES R. BOYCE, M.D., F.A.C.O.G.*

ABSTRACT

Between the years 1963 and 1972, eighty obstetrical patients were encountered at Hutzel Hospital with cervical carcinoma, an incidence of 0.16%. Seventeen percent of the patients were under the age of 24 years and the necessity of cytologic screening in this age group has been emphasized. Intra-epithelial carcinoma was practically asymptomatic in this group and detection was accomplished by vaginal smear and diagnosis confirmed by punch biopsy in 8%, cone biopsy in 85%, and cone biopsy followed by punch biopsy in 12% of the cases. The incidence of complications following diagnostic conization during pregnancy was 5%. Four patients had micro-invasive carcinoma, which was diagnosed by cone biopsy at between 36 and 39 weeks gestation and pregnancy was interrupted by means of Cesarean section. Unless childbearing functions were to be preserved, therapy consisted of Cesarean hysterectomy. Conservation of the ovaries depended on the age of the patient. Residual tumor in the hysterectomy specimen was encountered to be in the range of 62% and the implications of this have been emphasized.

Carcinoma of the cervix is being identified in association with pregnancy with increasing frequency and its management is assuming an increasingly important role in the practice of obstetrics. It is now a general assumption that carcinoma of the cervix can exist during pregnancy as an independent entity and that this process persists following termination of the pregnancy.[4] There is no evidence to show that pregnancy has an adverse effect on cervical cancer; however, its diagnostic and therapeutic management may have a significant effect on the outcome of the pregnancy, both fetal and maternal.[4] The widespread application of cytologic screening during pregnancy is the reason for the increasing recognition of the problem.[5] In view of this, it was thought worthwhile to review the experience with this problem during a ten-year period at Hutzel Hospital. This study was undertaken to determine the efficiency of diagnostic techniques and to evaluate the management of this lesion at this hospital. Particular emphasis was placed upon methods of diagnosis, type of treatment, and residual disease within the specimen.

Between the years 1963 and 1972, approximately fifty thousand deliveries occurred at Hutzel Hospital. Eighty (0.16%) of the patients had coexisting cervical neoplasms. Of these, seventy-five patients (94%) had carcinoma-in-situ of the cervix, four patients (5%) had invasive squamous cell carcinoma and one patient (1%) had sarcoma.

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RESULTS

Age Distribution

The age distribution among patients with intra-epithelial and invasive carcinoma associated with pregnancy is seen in Figure 1. The largest group of patients with intra-epithelial carcinoma ranged in age from 25-29 years (39%). This age distribution seems to be in accord with most reported studies. It is also interesting to note that in the present series, 17% of the patients were under the age of 25, again emphasizing the need for taking routine vaginal smears in this relatively younger age group and not relying on the age factor as an indication for commencement of cytologic screening.

Parity

The average parity in our study group was five. Of these, 37% of the patients had five or more children as can be noted in Figure 2.

Symptoms

Worthy of emphasis is the fact that the majority of the patients in the present study had no complaints. As TeLinde once said, "A true intra-epithelial carcinoma of the cervix has no symptomatology and any symptoms present may be attributed to other cervical pathology."[3] These patients were seen for routine prenatal care, at which time Papanicolaou vaginal smears were taken. Had it not been for a rigid cytologic screening program enforced in the prenatal clinic, the detection of intra-epithelial carcinoma in a significant number would have been delayed until symptoms appeared.

Diagnosis

All patients were screened by a Papanicolaou smear as can be seen in Table 1. Forty-seven percent had suspicious smears, 40% malignant smears, and 13% atypical smears. Diagnosis was confirmed by punch biopsy in seven patients, by cone biopsy alone in sixty-eight patients (85%), and punch biopsy followed by cone biopsy in ten patients (12%), Table 2. It is of interest to note that 13% of our patients had an atypical Pap smear and the question arises of whether patients with an atypical Pap smear should be subjected to cervical conization in spite of the presence of a normal appearing cervix. Pap smears provided the only evidence of abnormality leading to detection of carcinoma in our patients.

Complications associated with cervical conization should be anticipated; the incidence in the pre-

FIGURE 1

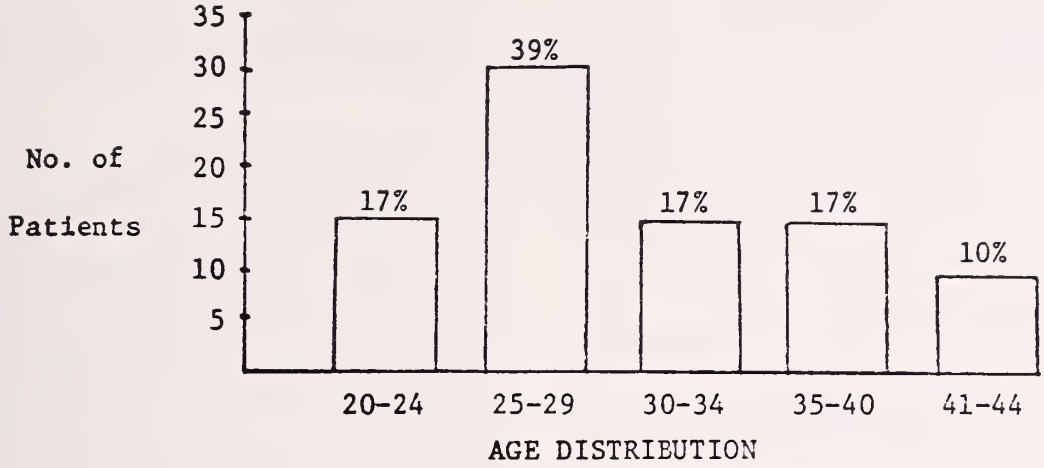

FIGURE 2

TABLE 1

CERVICAL CYTOLOGY		
Pap Smear	*No.*	*%*
Atypical	10	13
Suspicious	38	47
Malignant	32	40

TABLE 2

DIAGNOSIS		
	No.	*%*
Cone Biopsy	68	85
Punch Biopsy	7	8
Punch and Cone Biopsy	10	12

sent study was only 5%, Table 3. The most common complication was abnormal bleeding, which occurred in four patients. The other complication was premature labor, which occurred in one patient.

Pathology

Table 4 shows the Pathology report of the specimens submitted. Seventy-five patients (94%) had carcinoma-in-situ of the cervix, four patients (5%) had invasive squamous cell carcinoma, and one patient had sarcoma.

TABLE 3

COMPLICATIONS OF CONE BIOPSY		
	No.	*%*
Complications of Cone	5	7
Bleeding	4	
Premature Labor	1	

Method of Delivery

It is generally agreed that vaginal delivery should be permitted in all patients with intra-epithelial carcinoma, unless obstetrical complications indicate otherwise. In the present series, twenty-five patients (31%) were delivered vaginally, five pregnancies were terminated by Cesarean section, five had therapeutic abortions (mainly for psychological reasons), and forty patients (50%) underwent Cesarean hysterectomies, Table 5. The form of therapy for carcinoma-in-situ of the cervix would depend on the patient's age, parity, desire for more children, general health, and psychological factors. Patients who underwent Cesarean hysterectomies in our series did so after all of these factors were taken into consideration and the patients had the procedure because childbearing function was not a consideration. In these patients, it was thought that the lesion

Table 4

Pathology		
Type of Disease	*No.*	*%*
Carcinoma in situ	75	94
Invasive Carcinoma	4	5
Sarcoma	1	1

Table 5

Modality of Treatment		
Type of Delivery	*No.*	*%*
Therapeutic Abortion	5	6
Vaginal Delivery	25	31
Cesarean Section	5	6
Cesarean Hysterectomy	40	50

Table 6

Residual Tumor in Hysterectomy Specimen		
	No.	*%*
Cesarean Hysterectomy	40	100
Residual Tumor in Specimen	25	62
No Tumor in Specimen	15	38

had been removed by ante-partum conization. Fetal maturity was assessed either by ultra-sound or amniocentesis prior to the performance of the Cesarean hysterectomy.

Residual Tumor

Of the forty patients who were subjected to Cesarean hysterectomies as a definitive form of therapy for carcinoma-in-situ of the cervix, residual tumor was present in twenty-five (62%) and fifteen patients (38%) had no residual tumor in the specimen, as seen in Table 6. These findings should not be too surprising since a higher percentage of residual tumors should be anticipated in these patients due to the fact that during pregnancy the tendency is to perform a shallow cone in order to avoid the potential dangers of conization during pregnancy; thus not including all the perimeter of the carcinoma in the conization specimen. From this we can conclude that any treatment short of total hysterectomy should be reserved for the patient in the relatively rare and selected instance. This usually occurs in the young woman who strongly desires more children and is willing to return for examination and cytologic evaluation periodically. Even then, after a waiting period of several years, definitive surgical treatment is usually indicated.

Of the four patients with invasive squamous cell carcinoma, three had suspicious Pap smears and one patient had a malignant smear. Diagnosis was performed by punch biopsy in only one patient, and cone biopsy in the remaining patients at between 36 and 39 weeks gestation. Disease was staged as I-A and pregnancy interrupted by means of Cesarean section and treatment consisted of extended radical hysterectomy. In these cases, no residual tumor was found in the hysterectomy specimen.

The patient with sarcoma presented with a suspicious Pap smear. A punch biopsy of a polypoid lesion was performed in the clinic at 37 weeks gestation and reported as sarcoma. The patient underwent an extended Cesarean hysterectomy at 38 weeks gestation. No residual tumor was found in the specimen.

Comment

Although eighty patients is a small number for statistical analysis, we do, none-the-less, believe that certain tentative conclusions can be reached from this number of patients. The fact that most of our patients presented no symptoms, again stresses the importance of the Pap smear.

The search for cervical cancer should continue when the patient is pregnant.[8] Considering the fact that in its early stages, cervical neoplasm is asymptomatic, cervical cytology may be the most potent factor leading to the detection of cervical carcinoma, currently the most common gynecologic malignancy. Therefore, that the cytologic examination should be standard ante-partum procedure can hardly be stressed sufficiently. Cancer of the cervix in association with pregnancy need no longer be a tragic situation, difficult to manage, if adequate cytologic screening becomes an integral part of the practice of every physician in his prenatal care program. The typical patient with intraepithelial carcinoma of the cervix is one without symptomatology and has a normal appearing cervix which yields a suspicious or positive Pap smear.

Cold knife conization during pregnancy has been used to provide adequate sampling of the cervix. The dilemma "to cone or not to cone" still persists when one is confronted with a suspicious smear in pregnant patients, mainly because of the apprehension associated with it regarding complication.[3] In spite of this fact, it remains imperative that we utilize a diagnostic procedure necessary to properly evaluate the cervix before a patient is allowed to undergo labor and delivery by the vaginal route. The incidence of residual tumor in the hysterectomy specimen is surprisingly high and emphasizes several facts. First, it points out the inadequacy of cervical conization for those who consider this procedure both diagnostic and curative during pregnancy. Second, micro-invasive carcinoma is being diagnosed more frequently and, therefore, residual carcinoma is being diagnosed more frequently and, therefore, residual carcinoma might very well be micro-invasive.[1] Finally, it makes a difference during which trimester the cervical conization is performed. Cervical conization done during the third trimester is more likely to be incompletely excised because of the tendency to perform a shallow cone with residual tumor left behind. As shown in this study, there was a 62% incidence of residual tumor in the hysterectomy specimen.

Many problems in the future could be resolved by routine colposcopic examination of all patients with persistent suspicious or positive smears.[6,7] Many

Continued on Page 172

Percutaneous Transhepatic Gastroesophageal Varices Obliteration

A Case Report

PAYSON S. ADAMS, JR., M.D.*

It was often noted during percutaneous cholangiography that the portal venous system was frequently entered. In 1974, Lunderquist and Vang first described a technique of percutaneous transhepatic gastric coronary vein embolization. During preoperative workup of portal hypertension, they found the coronary vein was easily catheterized. Since 1974, more than 100 patients have been studied and treated utilizing this technique.

CASE REPORT

J. L., a 62-year-old obese male, was admitted to Mercy Hospital unconscious with hematemesis, blood per rectum, and ascites. The patient was anemic and diaphoretic. A Levine tube was passed and large quantities of bright red blood in the stomach was aspirated. The patient had a past history of a Bilroth I and vagotomy procedure for ulcer disease, and an alcoholic history. Endoscopy demonstrated large esophageal varices with bleeding at the lower end, probably in the stomach. No other gastric or duodenal abnormalities were seen. Liver function tests were relatively normal.

Six units of packed cells were infused in the first 2 days, but on the fourth day more aggressive bleeding ensued and five more units were given. IV Pitressin was started and then transfemoral superior mesenteric artery infusion was done. The bleeding began to slow and the patient improved. Two more units of blood were given over the next three days. Eight days later the patient began to massively hemorrhage and four units of packed cells and fresh frozen plasma were transfused over a short period of time. A Sengstaken-Blakemore tube was inserted but did not seem to decrease the hemorrhage. Because of the patient's unstable condition, his relatively rare blood type (A negative), and what may have been a potential blood shortage due to heavy snow from a nor'easter, percutaneous transhepatic gastroesophageal varices obliteration was done. After occlusion of the gastric coronary vein, the patient stopped his massive bleeding, but intermittently oozed over the next several days. He was waiting return of his albumin to a more normal level to undergo a shunt procedure, when seven days later the patient again began bleeding. He was given 4 units of packed cells, 4 units of fresh frozen plasma, and 10 units of platelets over a 24-hour period. He then underwent an emergency mesocaval shunt. Twenty-four hours later the patient again began to bleed and was given 7 units of packed cells, 20 units of platelets, and 2 units of fresh frozen plasma. During this time, a Sengstaken-Blakemore tube was again inserted slowing the blood loss. Clinically the patient appeared to have occluded the shunt. Endoscopy showed bleeding esophageal varices and no other pathology. Repeat venogram and re-embolization of the varices was undertaken. Portal pressure was found to be 43 cm. H_2O — about the same as before. The coronary vein was found to be recanalized and re-embolization was again radiographically successful, but blood loss did not seem to be well controlled when the Sengstaken-Blakemore tube was deflated. The patient underwent an emergency portocaval shunt and the bleeding stopped. At operation a large hematoma containing approximately one unit of blood was found in the abdominal cavity on the right side. Two units of blood and ascitic fluid free in the abdomen, obviously due to the obliteration procedure, were also found. Several small blood clots were found in the portal vein when it was opened. Over the next seven days the patient deteriorated, finally developing hepatic and renal failure and expired.

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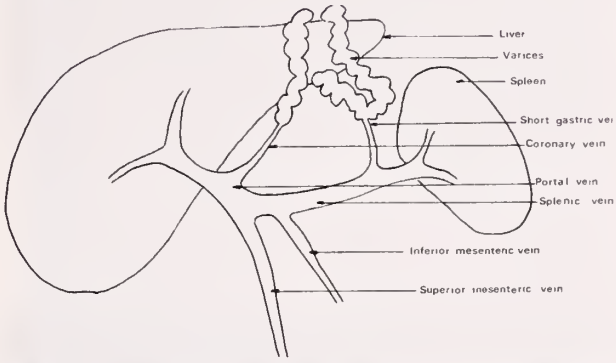

Fig. 1. Schematic drawing of anatomy of the portal venous system.

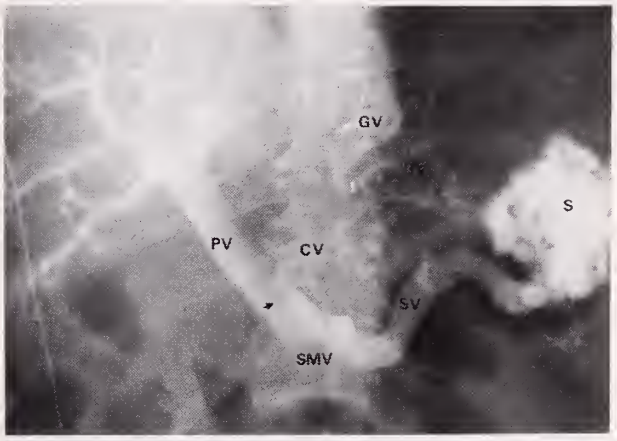

Fig. 2. Splenoportogram. GV — gastric varices. S — spleen. CV — branched coronary vein. SV — splenic vein. PV — portal vein. SMV — superior mesenteric vein. (Arrow marks dark streak of unopacified blood emerging from the vessel.)

METHOD AND DISCUSSION

The skin of the right lateral chest wall and upper abdomen is prepped and draped. A skin wheal with Xylocaine® is made just below the right costophrenic sinus in the mid axillary line at about the 10th intercostal space. After a stab wound is made, a #18 sheath catheter over a #19, 27 cm. Cook needle is advanced into the liver, angling down toward T-12 vertebra. The needle is withdrawn slowly. When free flow of venous blood is established, a test injection is made under fluoroscopy. A tight "J" .038

Fig. 3. Selective catheterization of the right limb of the coronary vein on first study demonstrating gastric varices and tributaries. Note inflated esophageal balloon of the Sengstaken-Blakemore tube.

Fig. 4. Almost complete occlusion of variceal feeders during first embolization.

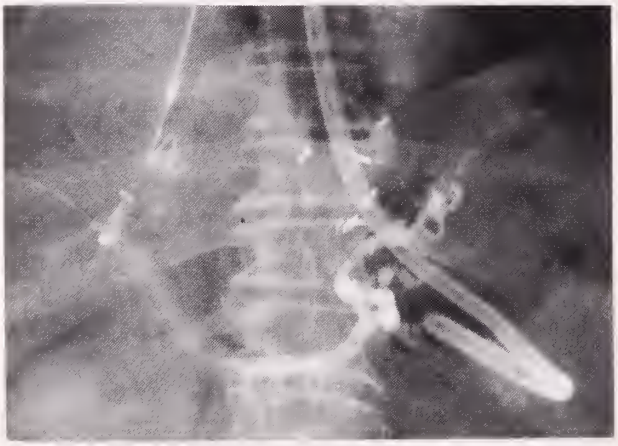

Fig. 5. During initial embolization, Gelfoam swept through system and vessels re-opened temporarily.

Fig. 6. Proximal branches of coronary vein occluded after first embolization.

Fig. 7. Splenoportogram after first embolization showing varices apparently occluded.

Fig. 8. Anatomy of the portal system with preliminary splenoportogram before the second embolization procedure. Note the mesocaval shunt is not open.

inch guide wire is inserted into the catheter and the entire system is advanced into the splenic vein where a venogram is made. This delineates the entire portal system demonstrating the varices and feeding vessels. In our case the patient was so obese that the sheath catheter could only reach the proximal splenic vein. It is possible that a short gastric feeding vessel could have existed. A change to a longer catheter over the guide wire can be done. This may not work, however, as the catheter may not follow the tract as the stabilizing guide wire is

Fig. 9. Varices demonstrated during second procedure. Note blood flow tends to feed toward the esophageal varices. Gastric varices may still be occluded, but flow has shunted toward the esophagus.

Fig. 10. Occulsion of the coronary vein following second procedure. Note several emboli in the intrahepatic portal venous system (Arrows).

much more flexible than the needle. New stiff wires have now been developed. Added instrumentation also increases the risk of complications. The portal pressure is measured before and after the procedure as successful embolization usually causes a rise in portal pressure on an average of 5 cm. H_2O.[1] The direction of blood flow is noted to see if it is diverted into the short gastric and coronary veins and into the varices. The catheter is then manipulated into the coronary vein utilizing a Cook deflector tip guide wire and obliteration attempted. Many embolizing agents have been used, but gelatin foam (Gelfoam®) alone is very effective. It is cut up into small 1x3 mm. pieces and using a guide wire or syringe pressure, pushed into the varices. Gelfoam alone was used for the first embolization, but a combination of Gelfoam mixed with a sclerosing agent (Sotradecol®) was used for the second attempt. This combination has been used extensively by Viamonte.[2] Some have used autogenous clot fearing Gelfoam may embolize through the varices, azygos system, and to the lungs. This complication, however, has not been noted. Expandable plastic sponges (Ivalon) have been used, as well as isobutyl 2-cyanocrylate which is not approved for use in the United States. Lunderquist and Vang[3] originally tried to create intimal damage of the vessel by injecting 30 ml. of 50% glucose followed by thrombin and Gelfoam injection. Guide wire intimal damage has been used, but may be dangerous.

After obliteration, the catheter should be readvanced into the splenic vein and another venogram done. This is done to identify if there is any short gastric vein contribution to the varices. If found, they should also be obliterated. One should try not to allow Gelfoam to reflux back into the portal veins of the liver, as occurred in our patient. What significance it might have is questionable. Frequent fluoroscopy should be used to follow the procedure, observing direction of blood flow. At completion of the study, the catheter is withdrawn to the edge of the liver capsule and a small amount of Gelfoam is injected to obliterate the catheter tract and reduce the chance of homoperitoneum. The large amount of blood loss in the abdomen in this case was compounded by the problem of ascitic fluid causing the liver to float away from the body wall. The tamponade effect of the liver against the body cavity was then lost. It was found that catheter manipulation was difficult because the catheter often coiled up in the space produced by the ascites between the liver and the abdominal wall.

No absolute contraindication exists as often the patients are exsanguinating. Platelet counts below

50,000 and prolonged prothrombin time should be serious considerations in selecting patients for obliteration procedures.

Results

The procedure is generally successful with either partial or complete occulsion occurring in about 90% of the cases. Statistics are variable on recanalization of the vessels, ranging any where from as high as 90%[1] to less than 10%,[2] but this could be related to the types and amounts of occluding agents used. If the patients are re-examined to evaluate whether vessels are recanalized, one must selectively catheterize the coronary vein to determine if it is actually occluded as splenic or portal venography alone can give one an erroneous impression as in Figure 8. At the very least, one must load the portal venous system with high volumes of contrast. Neither Lunderquist[1] nor Viamonte[2] mention what methods they used on re-study of their patients.

Most often hemostasis is achieved and the patient's clinical condition can improve enough to allow a shunt procedure. The shunt is the definitive method for control of bleeding over the long term. No recurrent bleeding has been reported in numerous patients following obliteration as the only mode of treatment.

Conclusion

In the case presented, the re-bleeding probably is evidence of recanalization, but it was felt that clinically the patient was more stable after the first procedure even in face of re-bleeding. It did not appear to be successful the second time. It is likely that the gastric varices were occluded, and remained so after the first obliteration procedure, while the esophageal varices opened and began to bleed subsequently.

Today experience is limited, but this procedure may become a more effective method of controlling gastroesophageal variceal bleeding than other forms of medical or invasive therapy in the initial stages of patient management.

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CERVICAL CARCINOMA DURING PREGNANCY — *Continued from Page 168*

cervical conizations could be eliminated. The diagnostic accuracy of the colposcopic-directed punch biopsy could probably yield more accurate results and solve the problem of whether or not to perform a conization.

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148 State St., Portland, Maine 04101

Brainstem Auditory Evoked Responses

WILLIAM H. LESCHEY, JR., M.D.*

Technological advances combine with ongoing basic and applied medical research to provide a steady stream of new diagnostic tests confronting, and sometimes intimidating, both the patient and the physician. A new test called Brainstem Auditory Evoked Responses (BAER's) or Far Field Brainstem Potentials has shown promise by revealing unique physiological information about the brainstem, a part of the central nervous system that heretofore has been difficult to study other than by the clinical neurological examination of the cranial nerves.

Computed tomography (CT Scanning) provides primarily anatomic or structural information and has limited applicability to study of the brainstem. The CT Scan may reveal a large brainstem hemorrhage, but is unrevealing in the more common patient with a demyelinative, ischemic, inflammatory or neoplastic lesion of the midbrain, pons, or medulla. Radionuclide (RN) or isotope brain scans fail to reveal evidence of any type of pathology confined to the brainstem. Conventional electroencephalopathy (EEG) has the limitation of not being able to sample directly brainstem electrical activity. The information about stem disease is therefore indirect, and the EEG patterns are nonspecific and non-localizing.

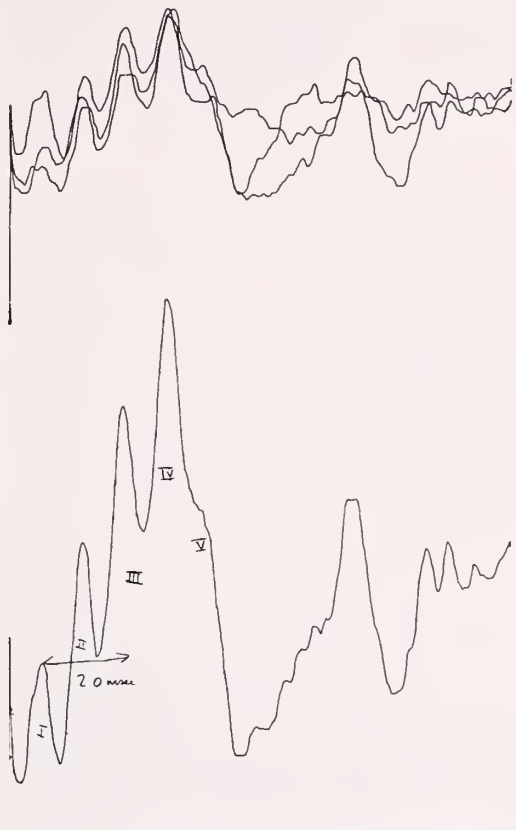

Fig. 1. A normal recording of brainstem potentials upon stimulation of the left ear. Note the highest amplitude of the IV, V complex. Interwave latencies of I to III, I to V and III to V measure 2.0, 4.2 and 2.2 milliseconds, respectively. Waves VI and VII are not labelled. The superimposed tracings above show the consistency from trial to trial.

CASE REPORT

A 33-year-old, 3 months pregnant woman, was recently admitted for evaluation of right sided facial numbness and severe vertigo associated with prominent autonomic symptoms. Two months prior to admission, she first developed numbness over the right lower lip. After several weeks, the numbness progressively spread to include the entire right trigeminal nerve distribution. Two weeks prior to admission, she began to experience vertiginous episodes, precipitated by movement, and associated with nausea and vomiting. She denied headache, hearing loss, tinnitus, and difficulty with balance except when acutely vertiginous. She also denied difficulty with chewing, diplopia, dysarthria and loss of coordination in the arms and legs.

The patient was gravida 3, para 1, and AB 1, and had no antecedent neurological history to suggest demyelinative disease. Her entire past medical history was in fact unremarkable.

On neurological examination, the patient had complete loss of pain and temperature sensation in right trigeminal nerve distribution. Touch sensation was preserved on the right side of the face. Trigeminal motor functions were unimpaired. There was no atrophy or weakness of the right temporalis, masseter, or pterygoid muscles. A mild conjugate gaze paresis to the right was noted. On attempted gaze to the right, a coarse, wide amplitude horizontal jerk nystagmus with an associated rotary (counter clockwise) component was evident. Downward gaze produced a primarily counter clockwise rotary nystagmus. On upward gaze, a mild horizontal jerk nystagmus to the right was present. A fine horizontal jerk nystagmus with fast component to the left was present on gaze to the left. All other cranial nerve functions including that of the auditory nerve were normal. No cerebellar deficits were present in the limbs. Gait was normal. No reflex changes were found. A complete ENT exam was also normal.

Initial workup included negative skull films with polytomes of the petrous bones, negative CSF exam including normal protein and gamma globulin percentage, normal audiogram, and negative RN brain scan. CT Scan without and with contrast enhancement was equivocal and non-diagnostic. Some minimal but suggestive widening of the right crural cistern was present. No mass was defined in the right cerebello-pontine angle or anywhere else. Visual evoked responses (VER's) and somatosensory evoked responses including short latency components were negative.

The BAER study was indicative of an auditory conduction defect in the caudal pons on the right. The left ear showed normal responses (Figure 1). The right ear showed an abnormally prolonged wave I to III interwave latency (Figure 2). A localized I to III abnormality is not the usual finding in multiple sclerosis. Prolonged III to IV, V interwave latency, or depressed voltage of the IV, V complex are the most common brainstem potential abnormalities in demyelinative disease.

The possibility of a neoplasm involving the right pons was raised. The patient had clinical findings of only a single lesion, and there was no laboratory evidence to support the diagnosis of multiple sclerosis. The patient declined further evaluation and was discharged. She was readmitted a few weeks later to another hospital where she was found to be dehydrated and have new neurological signs in the form of right trigeminal motor involve-

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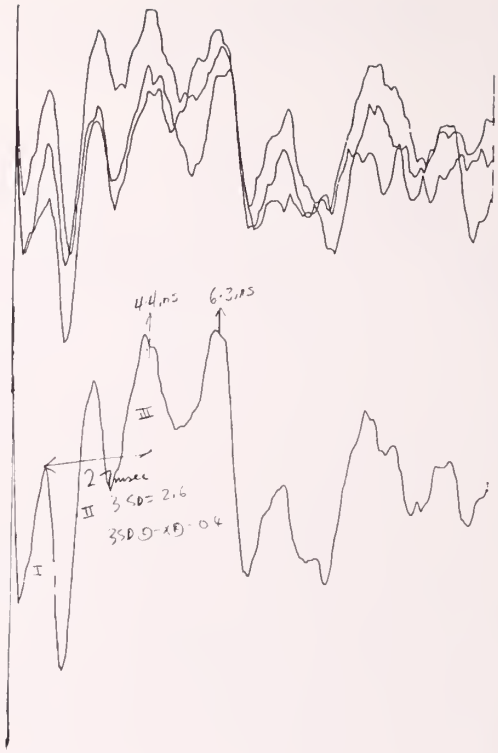

Right

Fig. 2. The responses upon stimulation of the right ear are abnormal. The interwave latencies of I to III, I to V and III to V measured 2.7, 4.6 and 1.9 milliseconds respectively. The I to III interwave latency is prolonged above 3 standard deviations in comparison to the other side and in comparison to normals.

Fig. 3. PA view of pneumoencephalogram showing right to left midline displacement of the fourth ventricle indicating a right cerebellar mass.

ment and ipsilateral cerebellar deficits. A pneumoencephalogram was performed and revealed a mass involving the pons and right cerebellum (Figures 3 and 4).

The patient subsequently had a suboccipital craniectomy. A Grade III astrocytoma involving the right cerebellum and infiltrating into the pons was found. After considerable discussion, the family decided to proceed with a therapeutic abortion. The patient is receiving postoperative chemotherapy and radiotherapy.

Discussion

In 1970, Jewett working with animals first discovered the short latency auditory evoked responses originating from electrical events occurring in the brainstem.[3] A short time later, he confirmed the presence of these waves in scalp recordings from humans.[4] A series of animal experiments followed, and were designed to correlate individual waves with specific structures of the auditory pathway in the brainstem. Subsequent clinicopathological studies of patients with brainstem pathology confirmed the findings of the animal experiments.[8,9] Although too simplistic for strict scientific or precise physiological interpretation, the seven waves correlate well with specific structures in the auditory pathway in an ascending order from the acoustic nerve to the auditory radiations:

Wave I = Acoustic Nerve
Wave II = Cochlear Nuclei (pons)
Wave III = Superior Olivary Complex (pons)
Wave IV = Lateral Leminiscus (pons)
Wave V = Inferior Colliculus (midbrain)
Wave VI = Medial Geniculate (thalamus)
Wave VII = Auditory Radiations (thalamocortical)

The wave IV and V appear frequently as a complex with several different morphological subtypes that are consistent from trial to trial and ear to ear in a given individual.

The seven waves all occur with latencies of less than 10 milliseconds and amplitudes less than one millivolt (100 times less than the voltage of a conventional EEG). Special techniques and equipment are required to record these potentials. Computer averaging permits enhancement of the time locked, low voltage waves relative to background noise. Three electrodes are placed on the scalp, one at the vertex (CZ of the 10-20 system) and two over the mastoids. Each ear is stimulated independently by a series of clicks presented through earphones. The term *Far Field* relates to the great (far) distance between recording site, the scalp, and the site of the electrical events, the brain stem. Optimal stimulation parameters have been detailed in early publications.[9] The potentials are measured from the vertex electrode to the ipsilateral mastoid upon monaural stimulation. Multiple trials are performed, the average test requiring approximately 45 minutes. A curve for each ear consisting of a series of vertex

Fig. 4. Lateral tomogram of pneumoencephalogram revealing marked posterior displacement of the fourth ventricle and aqueduct indicating an intra-axial pontine mass.

positive waves (by convention, an upward deflection) is computed, the waves being numbered in order of appearance from I to VII. Waves I, III, IV and V have been found to be the most useful in clinical studies.[2,7,9] The I to III interwave latency represents conduction through the caudal pons. Wave III to IV, V latency is a measure of pontine to midbrain conduction. A composite brain stem conduction is indicated by the I to IV, V interwave latency. Bulky computer equipment employed in early studies is being replaced by mircoprocessors. Portable equipment is in use, and becoming more readily available. The cost of this equipment is relatively low compared to CT scanners and other complex radiographic equipment that requires both higher initial capital and maintenance outlays.

Criteria of abnormality have been developed, and their validity verified in independent laboratories.[12] Interwave latency determinations are used to minimize effect of patient age, condition of the peripheral inner ear (cochlear) mechanism and variation in stimulation parameters. Amplitude criteria are also in use, and although of less help in general, are of increased usefulness when one ear is compared with the other, and when the amplitude of the waves is compared with that of waves IV or V, the waves of consistently highest voltage in normal subjects.

The clinical usefulness of BAER's is greatly enhanced by the failure of drugs to alter the interwave latencies. All drugs tested to date have had no significant effect on the brainstem potentials.[10] Unlike the flat or isoelectric EEG in the presence of severe barbiturate coma, the BAER's are normal in such a comatose patient. Toxic or metabolic encephalopathies do not affect the far field potentials, but can depress or abolish cortical activity generated by apical dendrites as displayed by conventional EEG. The patient brought to the emergency room in coma with no available history can be quickly determined to have structural brain stem disease if the BAER's are abnormal. This information has both therapeutic and prognostic implications.

Occult brain stem lesions not evident by clinical assessment or by non-invasive radiographic studies including CT scanning have been defined by BAER studies.[12] Both extra-axial and intra-axial posterior fossa tumors have been uncovered in symptomatic patients with negative neurological exams, normal audiograms, unremarkable CT and RN scans, and normal skull films with tomography. The brain stem potentials may be altered by an extrinsic tumor producing compression, or by an intrinsic tumor directly invading the auditory pathway. In the reported cases, the presence of the tumors was confirmed by arteriography, pneumography, pantopaque clivography, or neurosurgery.[12] The BAER study of patients with the cerebello-pontine angle syndrome has a high yield: acoustic neurinoma may produce early electrical abnormality when all other tests are negative.[1]

Several studies have focused on the BAER in multiple sclerosis (MS). These studies have produced similar results, testifying to the very high percentage of all MS patients that have abnormalities of brainstem potentials and confirming the usefulness of the test in establishing the diagnosis in patients with a solarity clinical lesion.[6,12] The most common abnormalities in MS are decreased amplitude of the IV, V complex and increased III to IV, V interwave latency. The primary benefit of the study to the MS suspect is derived from the elimination of the need for an invasive procedure such as myelography or arteriography. Although the therapy of MS remains unsatisfactory, establishing a definite diagnosis can be of help to the physician, patient and family.

Limitations of BAER studies are in the process of being defined. Several deficiencies are already apparent. If the patient has impaired hearing due to disease in the cochlea, unsatisfactory or misleading results might be obtained. Misinterpretation can be avoided if the cochlear microphonics are simultaneously monitored as part of the study. Some patients, however, with destroyed cochlear mechanisms will not have any brain stem potentials. No conclusions about brainstem function could be reached in such a case.

Hypothermia simulates structural brainstem disease by prolonging interwave latencies.[5] To avoid misinterpretation, the patient with a subnormal temperature should be warmed prior to study.

Gross brainstem pathology, which does not im-

pair the functional integrity of the auditory pathway, can be present in a patient with normal BAER's.[12] As applies to most laboratory tests, a negative study does not exclude significant pathology. A patient with a pontine or midbrain hemorrhage may have normal BAER's.

The brain stem potential studies share another feature in common with almost all other neurological diagnostic tests: The test provides information short of a definitive pathological or histological diagnosis. The physiological information provided, however, when integrated with the clinical findings and results of other tests can give very helpful clues as to the probable nature of the pathology. Invasive contrast studies incuding vertebral angiography, pneumography or patopaque clivography are most often required to provide additional information for the neurosurgeon prior to actual operation for posterior fossa tumor.

Technical and interpretive difficulties relating to equipment and recording techniques are considerable, and are by and large dependent on the sophistication and training of the technician and the electroencephalographer.

The relatively low cost, the uniqueness of the physiological information, the precisely localizing value, the non-invasiveness, the absence of drug effect, and the ability to uncover otherwise occult brain stem lesions seem certain to guarantee the success of this technique. Even greater use can be anticipated when therapeutic breakthroughs in the treatment of MS occur. Major or tertiary medical centers would be an appropriate setting for an evoked potential laboratory having the capability to perform BAER's.

In conclusion, the BAER represents a significant innovation in medicine and in the diagnosis of diseases of the acoustic nerve and brain stem. More widespread use seems almost certain. The procedure seems to be an appropriate screening test for patients with symptoms referable to the posterior fossa. The patient with dizziness, vertigo, nausea, vomiting, diplopia, oscillopsia, dysarthria, dysphagia, hearing loss, tinnitus, facial weakness or numbness, ataxia, singultus, coma or a large head (hydrocephalus) may be a candidate for BAER's.

Summary

A case of a pregnant woman presenting with a right pontine syndrome is reported. The BAER revealed a significantly increased I to III interwave latency, indicating a lesion in the right caudal pons. These electrical findings corroborated the clinical localization, and suggested tumor rather than multiple sclerosis as the etiology.

The history, methodology, clinical usefulness and limitations of far field brain stem potentials are discussed.

More widespread use of the technique seems certain, based on the relatively low cost, the ability to

Continued on Page 184

Tablets

Percodan® Ⓒ II

DESCRIPTION Each yellow, scored tablet contains 4.50 mg. oxycodone HCl (WARNING: May be habit forming), 0.38 mg. oxycodone terephthalate (WARNING: May be habit forming), 224 mg. aspirin, 160 mg phenacetin, and 32 mg. caffeine.

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone, aspirin, phenacetin or caffeine.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCODAN®, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCODAN® is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCODAN® should be cautioned accordingly

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCODAN® may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCODAN® should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCODAN® should not be administered to children.

Salicylates should be used with caution in the presence of peptic ulcer or coagulation abnormalities.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions The administration of PERCODAN® or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients PERCODAN® should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

Phenacetin has been reported to damage the kidneys when taken in excessive amounts for a long time.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient. The usual adult dose is one tablet every 6 hours as needed for pain

DRUG INTERACTIONS The CNS depressant effects of PERCODAN® may be additive with that of other CNS depressants. See WARNINGS.

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November 1977 EDO 149P

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1. Determine need

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3. Minimize potential risk

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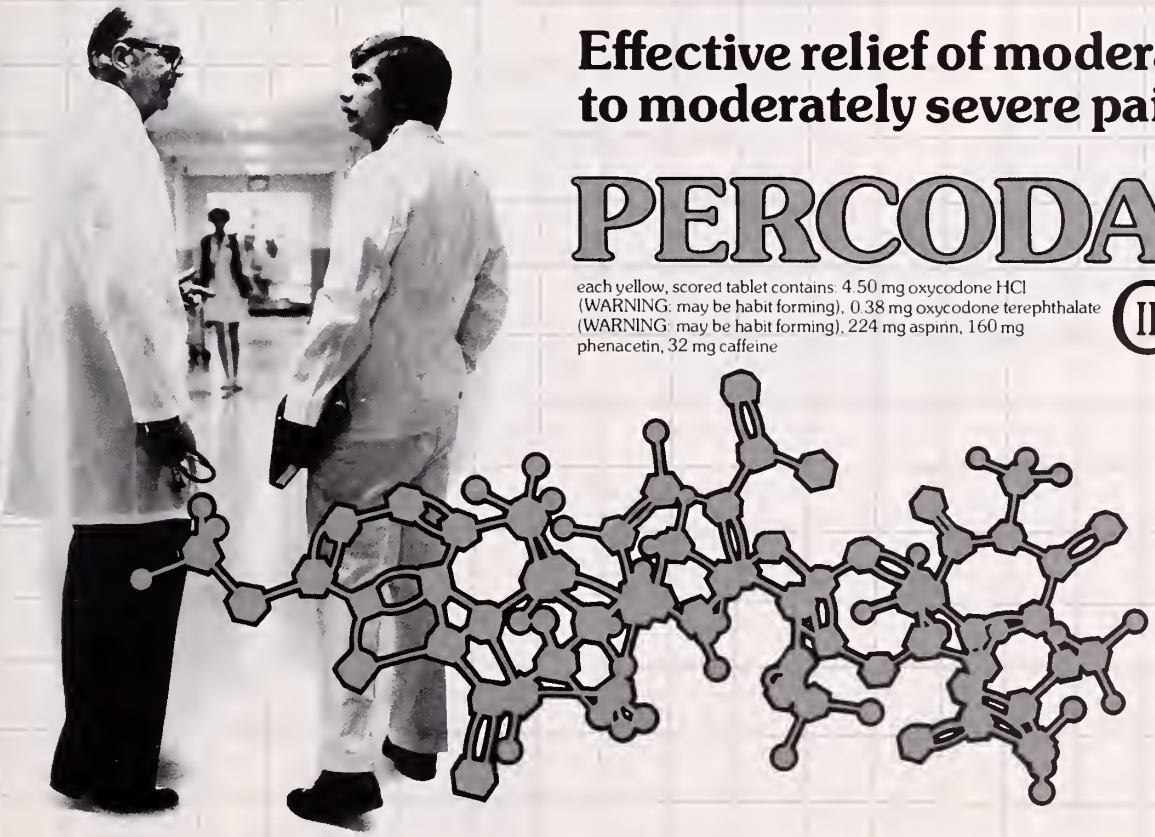
4. Provide adequate analgesia with minimum doses

Consider PERCODAN® because patients rarely ask for increased dosage. PERCODAN® relief can last up to six hours–until time for next tablet.



Effective relief of moderate to moderately severe pain

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CII

PERCODAN® is a registered trademark of Endo Inc.

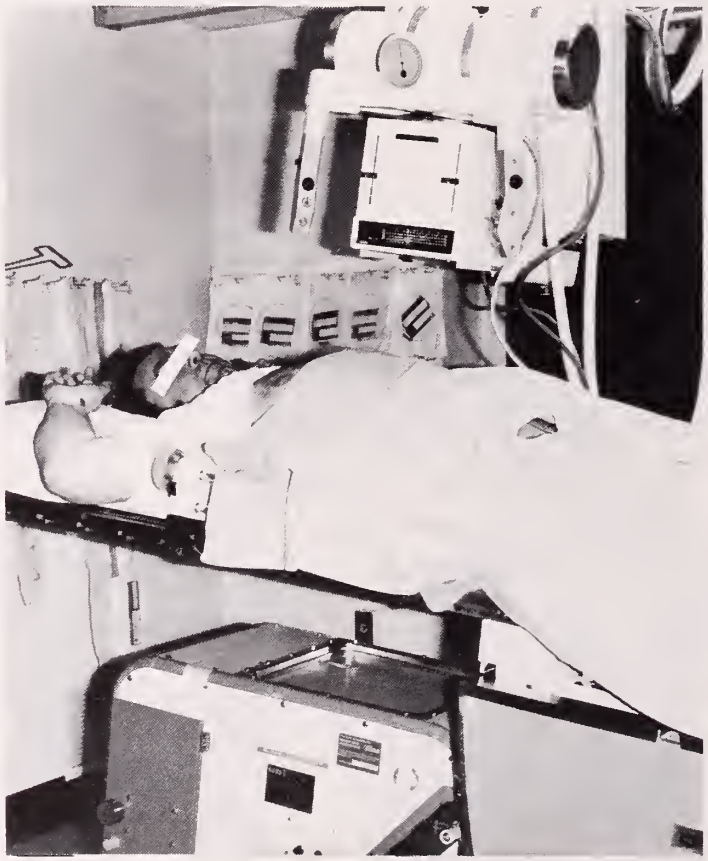
Please see facing page for Brief Summary of prescribing information.

Magnification Renal Angiography With a Standard Fluoroscopic Table

Technical Note

LAURIE J. MURRAY, R.T.* and PAYSON S. ADAMS, M.D.**

In many smaller institutions the angiographic suite must also double for routine fluoroscopic examinations. An adjustable height angiographic table is usually not available, therefore magnification studies of the kidneys are not done. These films can be obtained, however, with a tilting fluoroscopic table. The table



top is extended over a floor mounted rapid serial film changer (at our institution an AOT Schonander is used). The table is then tilted to place the patient in reverse Trendelenburg position of 10°. The film changer and overhead x-ray tube are angled to 10° also to maintain parallel planes. Maintaining a focal-film distance of 40 inches (100 cm.), the table top is extended to place the kidney being examined in the center of the film. An object-film distance of 20 inches (50 cm.) and a focal-object distance of 20 inches (50 cm.) is obtained resulting in a 2X linear magnification. This technique has been used at our institution with success. A fractional focal spot of 0.3 mm. and a non-grid air gap technique with tight collimation were used to achieve films of good quality.

*Special Procedures Technologist, Mercy Hospital, Department of Radiology, Portland, Maine 04101.
**Radiologist, Mercy Hospital, Department of Radiology, Portland, Maine 04101.

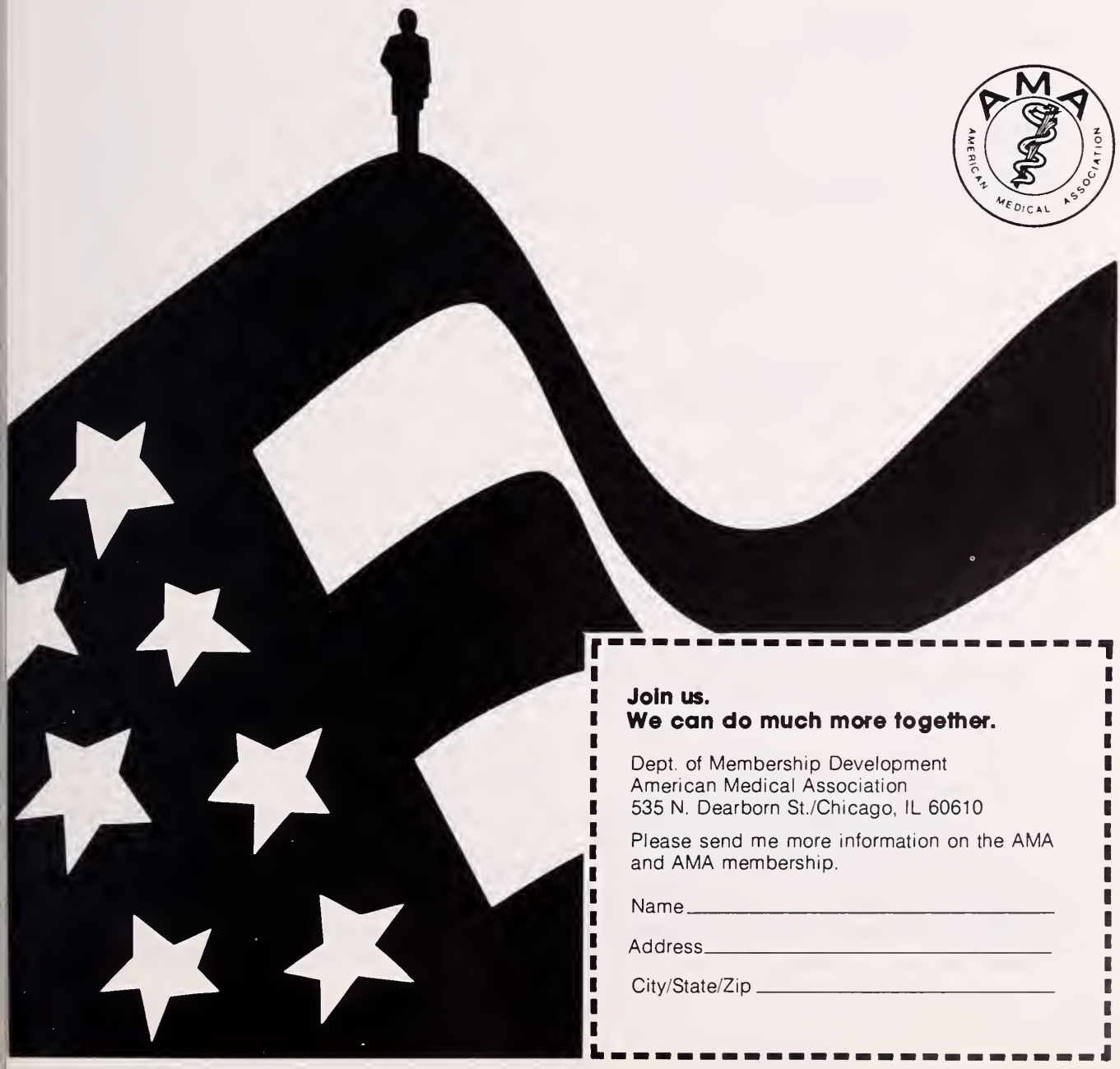
Medicine's men on the Hill

Just who are they? They're the AMA's permanent representatives to the Congress of the United States from the AMA's Washington office.

In every Congress about 10% of all legislation introduced is health related — some 2,500 bills and the number is increasing every year. The AMA lobyists serve as the profession's eyes, ears, and voice on the Hill. Keeping in day-to-day contact with the members of Congress and their staffs. Explaining and promoting the profession's views. Reporting on legislation. And providing legislators with resource material and information on medical and health subjects.

They're on the Hill to protect your interests, lobbying to retain the basic freedoms of medical practice in any government health program that might be enacted. Equally important, they lobby to insure the passage of constructive and workable health legislation for the public.

Sure, the AMA lobbies. It lobbies for the rights and interests of our profession and for quality medical care for every American. With your support, the AMA can be even more effective.



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HEALTH COSTS DISCUSSION DOMINATES ANNUAL MEETING

Good health at reasonable prices is within the grasp of most individuals. That was the message issued by Richard J. Stride, Chairman of Blue Cross and Blue Shield's Board of Directors, at the organization's annual meeting on April 19th. Stride, in his statement to the Board, said, "When it comes to good health, it is the individual and family, not the hospital or the physician, who ultimately controls the outcome. And at a fraction of the cost."

"The truth is that most of us know too little about or tend to be indifferent to the many factors of everyday life that affect our bodily and mental well being. By adopting certain habits of living . . . diet, exercise, general life style, we actually determine not only how and from what, but even when, we will die. We spend millions of dollars a year in Maine to repair the unfortunate consequences of the self-inflicted abuse inherent in unhealthy life styles," said Stride.

Business at the annual meeting included the election of nine members to the Board of Directors. Re-elected for 3 year terms were the following: Representing consumers — Perham Amsden, P. Harold Albair, Lloyd Holmes, and Doris Karter; representing Participating Providers — George Avery, Fletcher Bingham, and Derek V. Bush; and representing Participating Professionals — Lewis Estabrooks, D.M.D., H.E. Knuuti, M.D., and Frederick Schwartz, D.O. John A. Mitchell was also elected to serve as Clerk for one year.

Special awards for past service to the Board were presented to Warren Kessler (for 5 years of service), John Jackson (9 years), and Benjamin Dorsky (19 years).

Officers' reports were also heard at the meeting. Retiring President, Richard F. Nellson, pointed out that Blue Cross and Blue Shield of Maine has grown from 368,000 members in 1964, when he became Chief Executive Officer, to over 551,000 members today. In 1964, over $15 million in subscriber benefits were paid out. During 1977, that figure rose to over $82 million, an increase of 447% over a fourteen year period.

Nellson's successor as President, George E. McLean, said in his report, "I recognize that we have already entered a critical era, wherein we will have to find ways to meet Maine's health needs without breaking the bank in the process. Our goal for the future is to work with health planning agencies, healthcare providers and professionals, our consumer councils, and our subscribers toward one common purpose . . . the good health of Maine people at a cost they can afford."

George Hansen, Treasurer of the organization, noted that inflation and other increases in the cost of health care continued to provide the predominant impact on the financial results of operations of Blue Cross and Blue Shield of Maine in 1977. The total volume of health care dollars administered on the behalf of Maine citizens (including Medicare Part A) reached another new high of $186,825,000 which represented a $32,156,000 (21%) increase over the $154,669,000 processed in 1976.

On a combined basis, Blue Cross and Blue Shield returned in benefits almost 93¢ for each dollar of subscription income earned and placed another 3¢ in reserve to maintain the combined reserves at 2.68 months of claims plus operating expense compared to 2.66 months at December 31, 1976. The reserve of 2.68 months at year end, which amounts to $30.68 per Blue Cross member and $5.16 per Blue Shield member, compares favorably with the reserve range of two to three months required by the Bureau of Insurance.

News, Notes and Announcements

4th Annual Seminar on Sports Medicine Maine Maritime Academy Castine, Maine June 25-28, 1978

Accreditation: This Conference is acceptable for 13 hours Category II credit from the AMA, and the AOA, 1.3 CEU's from Maine Maritime Academy, application has been made for NATA approval.

For further information contact, Len Tyler, Coordinator, Summer Programs, Maine Maritime Academy, Castine, Maine 04421, Tel.: (207) 326-4311, Ext. 254.

Office Dermatology Course Offered

The American Academy of Dermatology, Colby College and Mid-Maine Medical Center will sponsor the Second Annual Seminar in "Office Dermatology" August 1-4, 1978 at Colby College, Waterville, Maine.

The seminar is designed for primary care physicians who treat patients with dermatological disease in both office and hospital. Emphasis will be placed on correct diagnosis and treatment of the most common skin disorders. The course will provide an overview of advances in dermatology and will detail current concepts in diagnosis and patient care. The teaching format will include in-depth and short presentations, motion pictures, panel discussions, and questions from the audience.

As an organization accredited for Continuing Medical Education, Colby College certifies that this continuing medical education offering meets the criteria for 14 credit hours in Category I of the Physician's Recognition Award of the American Medical Association, provided it is used and completed as designed. This program is acceptable for 14 elective hours by the American Academy of Family Physicians.

Tuition for the course is $150. A deposit of $50 should accompany each application for registration. For further information, contact: Department of Continuing Medical Education, American Academy of Dermatology, 820 Davis Street, Evanston, IL 60201.

29th Annual Session American Association for Laboratory Animal Science September 24-29, 1978 New York Hilton Hotel New York, NY

For information contact: Mr. Joseph J. Garvey, Executive Secretary, AALAS, 2317 W. Jefferson St., Suite 208, Joliet, IL 60435.

30th Annual Workshops and Scientific Program of the Society for Clinical and Experimental Hypnosis

The 30th Annual Scientific Program and Workshops of the Society for Clinical and Experimental Hypnosis will be held at the Grove Park Inn in Asheville, North Carolina (in the Blue Ridge Mountains of the Great Smokies) from Tuesday, October 17th through Sunday, October 22nd, 1978. The meeting will be cosponsored by the Department of Psychiatry, the Department of Anesthesiology and the Department of Psychology of the University of North Carolina; the Office of Continuing Education, University of North Carolina School of Medicine, and the Office of Continuing Education, University of North Carolina School of Dentistry.

At least ten workshops will be offered including Introductory and Advanced Medical, Psychotherapy, and Dental. There will also be a special workshop for psychiatric residents, two Research Workshops, one for psychologists and psychiatrists and the other for doctoral candidates, a Workshop on Self-Hypnosis and the Control of Pain, and one on The Clinical Use of Hypnosis with Children.

For further information and registration forms write to: Marion Kenn, Administrative Director, S C E H, 129-A Kings Park Drive, Liverpool, New York 13088.

Antivenin Index Center

The Antivenin Index Center is a current catalog of snake-bite antivenins stocked in North American zoos, laboratories and related institutions. The Center provides a 24 hour-a-day retrieval service on antivenins available for the treatment of venomous snake-bite from native and exotic species. The Index is limited to sera currently stocked by participating institutions. Also, full data is provided on telephone numbers and personnel to obtain emergency supplies of antivenins.

The Center does not stock antivenin; rather, it serves as an index for emergency information on available antivenins.

To Use This Service . . .

1. Obtain both the scientific name (genus and species) and the common or vernacular name of the snake involved (e.g., Dendroaspis polylepis, Black mamba). Knowledge of the correct scientific name is almost indispensable in the proper selection of the appropriate antivenin.
2. Call the Antivenin Index Center in Oklahoma City, 405/271-5454 for the following information:
   - Antivenins applicable to your snake-bite which are currently stocked in North American institutions.
   - Locations of available stocks nearest to you, amounts currently in stock and expiration dates.
   - Emergency telephone numbers and names of key personnel for obtaining the antivenins from the listed institutions.
3. Contact your nearest supply and make arrangements for emergency delivery of antivenin.

Colleagues Honor Dr. Blaisdell

A veteran Portland physician and the dean of Maine's diabetes specialists was honored by colleagues April 26 with a program at Maine Medical Center billed as "Elton R. Blaisdell Diabetes Day."

Highlights of the all-day session were a testimonial address entitled "Dr. Blaisdell — Physician and Leader in Maine Medicine," delivered by Dr. Stanley Herrick of Lewiston, and the first Elton R. Blaisdell Lecture, "Recent Developments in Diabetes," by Dr. George Cahill, director of the Elliot P. Joslin Laboratory, Boston, world center of diabetes research.

Dr. Blaisdell was a pioneer in the modern treatment of diabetes, practicing in Portland for nearly half a century. He is a native of Westfield and a graduate of Aroostook Central Institute and Bowdoin Medical School with subsequent study of diabetes mellitus at Harvard Medical School and in Germany and Austria. He served as chief of medicine and has been a member of the MMC consulting staff since 1959.

Citizen Award Announced

Dr. Joseph Mendes, of Lisbon Falls, was named "Outstanding Citizen" by the Lisbon Rotary Club during the club's Spring Ball at the Lewiston Memorial Armory recently.

Dr. Mendes, a family physician in Lisbon Falls for more than 20 years, was chosen as the first recipient of the Rotary Club's new award because of his "many years of service to the Lisbon community and his untiring participation as a coach and booster of the community's youth sports program," according to a club spokesman.

Letter to the Editor

To the Editor:

We are sure that you are aware of the definite health risks of smoking during pregnancy such as low infant birth weight, increased perinatal mortality, and impaired long term physical and intellectual development. Women who smoke have *twice* the risk of delivering low birth weight infants as women who do not smoke. If, however, a woman can quit smoking by the fourth month of pregnancy, her risk of a low birth weight delivery is similar to a non-smoker.

As a first step to combat the problem of smoking during pregnancy, the Bureau of Health is requesting the help of Maine's hospitals in collecting baseline data on the severity and extent of smoking among women delivering in Maine. We would like to inform you of this survey and express our appreciation for the support and cooperation we have received from your members.

WILLIAM NERSESIAN, M.D.
State Epidemiologist
State of Maine
Department of Human Services
Augusta, Maine 04333

County Society Notes

Lincoln-Sagadahoc

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held on February 21, 1978 at The Ledges Inn in Wiscasset.

Twenty-two physicians attended the meeting which was called to order by the President, Dr. Aldo F. Llorente, at 8:10 p.m., after dinner.

Nomination of an internist to serve on any proposed arbitration panel was postponed.

Dr. William Nersesian, State epidemiologist, spoke on the study of the pattern of natural history of disease.

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held on March 21, 1978 at The Ledges Inn in Wiscasset.

Twenty-seven members attended and stood in silent respect in memory of Dr. John F. Dougherty, of Bath, recently deceased. The secretary was directed to write a letter of encomium to Mrs. Dougherty.

Dr. David W. Schall presented a synopsis of the M.M.A. House of Delegates interim meeting and Dr. Richard C. Leck made additional comments on proposed premium rates of the sponsored physician-owned professional liability insurance company.

Members commented on the reporting of C.M.E. hours as prerequisite for both M.M.A. membership and continuing licensure.

Dr. Henry Ryan, Chief Medical Examiner of the State of Maine, spoke on the M.E. system and showed illustrative slides.

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held on April 18, 1978 at The Ledges Inn in Wiscasset.

Seventeen physicians were present and approved old minutes and discussed a letter from Dr. John P. Dow of Pittsfield requesting the name of a political activist from among the members. There was much discussion but no name.

Dr. Richard C. Leck spoke on professional liability insurance and introduced Mr. John Schroeder, of the firm of Johnson & Higgins, who expatiated on the current status of the Medical Mutual Insurance Company of Maine.

GEORGE W. BOSTWICK, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association met at John Martin's Manor Restaurant on March 16, 1978, with 42 members and 3 guests in attendance.

The meeting was called to order by the Vice President, Dr. Valentine J. Moore, in the absence of Dr. Richard E. Barron at 8:30 p.m.

The minutes of the previous meeting were approved as read.

Under old business, Dr. Feagin corrected a mistake in the Treasurer's Report which he had submitted last month.

New Business: The applications of Drs. Herbert Bartholomew, Clifford Nemeth and Alexander Wall were read at the first reading.

Dr. Moore then introduced our speaker, Senator Richard Pierce of Waterville, who is Chairman of the Select Committee on Rural Health and Medical Education. Senator Pierce discussed with the members of the Society the active legislation of special interest to physicians and most especially discussed the medical compact legislation. There was a brief question and answer period and the meeting was adjourned at 9:15 p.m.

O. THOMAS FEAGIN, M.D., *Secretary*

Penobscot

The March meeting of the Penobscot County Medical Society was held on March 21, 1978 at the Airport Hilton in Bangor.

The meeting was opened by the President, Dr. Philip G. Hunter. The minutes of the February meeting were approved. It was announced that the Medical Mutual Insurance Company of Maine is in the process of organization. LD 1997, the bill giving legislative support to the insurance company, was recently enacted and signed into law by the Governor. The actuarial consultant firm of Johnson and Higgins recently suggested to us that the premiums will be in the range of 40% to 50% of what one would be paying to the JUA in his class.

The applications for membership of Drs. Joan MacCracken and Harold Veits were presented and unanimously approved. A third application from a Dr. Allen was discussed; formal voting was deferred until Maine medical licensure has been obtained by the applicant.

Dr. Bradley Brownlow, from Blue Hill, then spoke to us regarding the Health Systems Agency. Dr. Brownlow is one of the original members of the sixty-nine Board of Directors of the Agency. He discussed the formation of the HSA, how it functions and relates to the other health planning boards in the State. He presented the recently developed Health Systems Plan, which is a five-year plan for the State of Maine; he also mentioned the yearly, annual implementation plan. A brief question and answer period followed.

The meeting was adjourned at 9:45 p.m.

H. CLEMENT JURGELEIT, M.D., *Secretary*

Washington

A regular meeting of the Washington County Medical Society was held at the Medical Staff Lounge of the Down East Community Hospital, Machias, Maine on April 13, 1978, with eleven members and guests present. Dr. James C. Bates, Eastport, President of the Society, presided at the meeting.

I. Dr. Douglas R. Hill, President of the Maine Medical Association, spoke on the many problems facing the Medical Association.

a. Question of the Association moving their headquarters from Brunswick to Augusta, or somewhere nearby. This would create many problems, not only financially, but a question of M.D. supervision. At present with Dr. Hanley's office being above the Association rooms, it is relatively easy for him to keep abreast of new developments. If a move is made, officers of the Association would have to spend more time supervising the Assistant Executive Director; or, as it was suggested, perhaps an M.D. from the University of Maine, Augusta, Maine, could take this supervision as a part-time job, and still not be out of touch with medicine.

b. Dr. Hill mentioned the Maine Medical Joint Underwriting Association has been set up by doctors. This group is ready to go. A company has been formed; the policies will be issued by July 1. It will be a mutual type of company and it is expected it will cover the doctor when he has retired. It hopefully will be less expensive than the present plan, since the rates would reflect Maine rates, rather than rates coming out of a State like California.

c. Dr. Hill also said that Certificate of Need Legislation has been passed, but doctors' offices had been excluded.

II. *Report of House of Delegates:*

a. Dr. Robert G. MacBride, Delegate to the Maine Medical Association, reported on the recent meeting of the House of Delegates.

b. Dr. MacBride stated that Dr. Hill had covered most of the things taken up at this meeting and he again emphasized the Maine Physicians' Malpractice Insurance organization.

III. *Washington County Health Plan:*

a. Dr. Robert G. MacBride discussed the WCHP. He stated that he had a telephonic confirmation that the present plan would be funded for another year. This was followed by considerable discussion of the new WCHP grant proposal.

b. A motion was made and seconded that the Washington County Medical Society express disapproval of the new grant proposal of the Washington County Health Plan.

1. The eight (8) members present voted by ballot, against this plan. The other members of the Medical Society will be polled, to get their views, before the motion is passed.

IV. An excerpt of the WCMS meeting of August 4, 1923 was read. "The WCMS met at the Algonquin Hotel, St. Andrews, N.B. and listened to a talk by Dr. Charles Best of the University of Toronto. He gave an address on Insulin, its history; its production; its administration and its affects." The following letter was sent to Mrs. Charles H. Best: "Dear Mrs. Best: The members of the Washington County Medical Society learned with deep regret of the passing of your husband, Charles. I am Secretary of the Washington County Medical Society, and I have custody of the Secretary's reports. On looking back in the files, I found where Dr. Charles H. Best of the University of Toronto, spoke to the WCMS on August 14, 1923, at the Algonquin Hotel, St. Andrews, N.B. He spoke, of course, on Insulin. I understand that your husband also attended many other meetings of the County Society. My late father, Oscar Larson, M.D. of Machias, Maine was very active in the Medical Society. He often times spoke of your husband and of his father, H. H. Best, M.D. I had the honor of meeting Dr. Best, myself, at various times when he was here during the summer months. He was always regarded as one of the Counties' outstanding sons." This was signed, Karl V. Larson, M.D., Secy. of WCMS.

V. *Discussion of Down East Health Service Agency:*

It was the general feeling of the Society, though set up by physicians, it has taken over many activities that formerly were the prerogatives of physicians, and that in general it needs somewhat firmer control, particularly in the type of information it is giving to patients.

a. A motion was made by Dr. G. Bernard Shaw and seconded by Dr. John Kazutow that the Medical Society appoint one member to the Board of Down East Health Service. James Payson, D.O. of Machias, Maine was nominated by the Medical Society to be their representative to the Down East Health Service.

KARL V. LARSON, M.D., *Secretary*

Androscoggin

The April meeting of the Androscoggin County Medical Association was held on April 20, 1978 at No Tomatoes.

The meeting was called to order by the President, Dr. Jou S. Tchao, with 46 members present and two guests. A social hour and dinner preceded the meeting. Mr. James McLoughlin, public relations director of the Maine Medical Association, spoke briefly.

The speaker of the evening was Mr. A. Douglass Scott, the sales representative of Dumont Industries, of Monmouth, Maine. He was introduced by Dr. Lawrence A. Nadeau. Mr. Scott gave a most informative talk on Solar Energy Systems and Heat Saver Solar Equipment. A question and answer period ensued. There was literature for interested members.

The business meeting was opened at 8:50 p.m. by Dr. Tchao. The secretary's report was accepted as presented.

A transfer of membership application of Dr. Walter R. Peterlein, Jr. from York County to Androscoggin County was approved and voted on favorably.

Copies of the budget for the Maine Medical Association were distributed to the membership and discussed.

Following discussion of the lobbyist for the M.M.A., Dr. Behzad Fakhery moved that the lobbyist should represent only the physicians and not divide his time with other matters which many times conflict with the physicians' problems. The motion was seconded by Dr. Victor M. Parisien and duly voted.

Dr. Tchao gave information on the Telephone Answering Service and Mobile Radio cost. No action was taken.

Other correspondence from Dr. Thomas F. Shields was postponed due to the fact that Dr. Shields had to leave the meeting.

It was voted to hold the May meeting at Lost Valley on May 21, 1978.

It was voted to hold the September meeting at Bates College, Chase Hall and to have a sit-down dinner.

It was left to the executive committee to consider additional compensation for Juliette, the assistant secretary.

Meeting adjourned at 9:20 p.m.

KENNETH P. WOLF, M.D., *Secretary*

Oxford

A regular meeting of the Oxford County Medical Society was held on April 12, 1978 at the Mexico Chicken Coop, Mexico, Maine, with twenty-one, including one senior member, present.

The Vice-President, Dr. H. Richard Bean, called the meeting to order at 6:30 p.m.

The reading of the minutes of the last meeting were dispensed with on motion made by Dr. William L. Medd and seconded by Dr. Harry L. Harper.

Old Business:

Discussion ensued in regard to the continued membership of a physician who is no longer a resident and who had defaulted. It was suggested that the secretary check the Rules and Regulations of the Oxford County Medical Society relative to this matter and report at the next meeting.

New Business:

The application of Dr. William T. Whitney, Jr. for membership was approved unanimously by the members.

Dr. Medd informed the Society of "ROMED" Clinical Cardiology Conferences which will be conducted at Stephens Memorial Hospital, Norway, from May 1 through May 5, 1978. This program is authored by Dr. W. P. Harvey and the program meets the criteria for 10 hours of CME Category I credit. Dr. Medd also informed the Society of a new insurance company which will start operation in July of this year. Prospectus will be

made available soon.

A communication regarding neonatal problems was also discussed.

A letter from Dr. John P. Dow, Chairman of the Maine Medical Association Legislative Committee, was forwarded to the Society President in regard to physician contacts for legislators. The secretary will respond to Dr. Dow's letter and will forward him a copy of the list of physicians agreeing to serve as contacts from the Society.

Following adjournment of the meeting, an excellent dinner was served.

HARBANS S. SODHI, M.D., *Secretary*

BRAINSTEM AUDITORY EVOKED RESPONSES — *Continued from Page 176*

uncover occult brainstem lesions not revealed by other non-invasive tests, and the uniqueness and physiological nature of the information provided.

ACKNOWLEDGEMENTS

Keith Chiappa, M.D. at the Massachusetts General Hospital performed the BAER's in the case reported. Samuel M. Wolpert, M.D. at New England Medical Center Hospital performed the pneumoencephalogram. Kalmon D. Post, M.D. at New England Medical Center Hospital performed the surgery.

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County Society Notes

York

The March meeting of the York County Medical Society was held on March 8, 1978 at the H. D. Goodall Hospital in Sanford, Maine. The program started off with a social hour from 6:30 p.m. to 7:30 p.m. at Dr. Vachon's office.

The dinner, talk and business meeting followed.

After an excellent meal, we were fortunate in having a most interesting and knowledgeable speaker. He was William Newman, J.D., C.P.A. of Portland, Maine. His subject was "What the Physician Should Know About Income Taxes." This talk was replete with questions and answers and was one of the most actively involved ever.

Following the speaker, Dr. Lawrence Hazzard, President of our Society, called the meeting to order. The minutes of the Annual Meeting were dispensed with, in the interest of time. There was no old business of interest.

New business brought forth a resolution by Dr. Irvin Dorfman, which had the unanimous approval of all the physicians present, and was so voted. This resolution is to be presented at the House of Delegates interim meeting of the Maine Medical Association held at the Eastern Maine Medical Center, Bangor, Maine on March 18, 1978.

For your information, the resolution is as follows:

WHEREAS, reimbursement for medical services has been assumed largely by third party agencies,

WHEREAS, grievances concerning fee levels, turnaround time of claims, eligibility, etc. are becoming increasingly difficult to gain a fair hearing,

BE IT RESOLVED, that the Maine Medical Association establish an office to receive, document and arbitrate complaints of Physicians regarding their relations with third party payors, there being currently no other resources available except the courts of law.

Another item was the application of Dr. Robert Kammerman which was presented for induction into our Society. It met with unanimous approval and he was duly elected into membership.

The following announcements were made:

The next meeting of the York County Medical Society, to be held at the Webber Hospital, Biddeford, on Wednesday, May 10, 1978.

The Diabetes meeting to be held at Nasson College on April 29, 1978.

House of Delegates meeting at Bangor, Eastern Maine Medical Center on March 18, 1978.

There was no correspondence or miscellaneous business of interest.

There were 17 physicians and 2 guests present. There was the usual dirth of attendance. The meeting was thereupon adjourned.

MELVIN BACON, M.D., *Secretary*

Aroostook

The regular meeting of the Aroostook County Medical Society was held at the Northeastland Hotel on March 15, 1978.

The meeting was called to order by the President, Dr. Arthur D. Pendleton, with 18 members present. Minutes were read and accepted.

The question of revision of the Society's bylaws to bring them into agreement with the Maine Medical Association was raised. After some discussion, it was decided to appoint a committee at a later date to look into the matter.

Legislative action including the pending Certificate of Need bills were discussed. The pending malpractice insurance bill and the status of the 10% Medicaid fee reduction also came up for comment by the membership. No formal motions were made.

Dr. J. B. Leith Hartman reported on a recent meeting he attended concerning various cancer treatments including Laetrile and commented on the carcinogenic effect of red dye.

The Treasurer's report was read and accepted and placed on file.

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		1979
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The Journal
of the
Maine Medical Association

Volume Sixty-nine | Brunswick, Maine, July 1978 | Number 7

"Night Watch"

MERRILL J. KING, JR., M.D.*

I

It darkens now.
The sun's last glow has faded in the west
Where in topaz splendour gleams bright Venus,
planet of the evening.
Visitors come and go, 'midst words of empty cheer.
"Be seeing you Charlie", "How ya' doing, Joe?",
"You look great!"
(Betty sends her regards.)
Some really seem to care, and some do comfort.

The evening meal is done, and the stream of sick and
would-be sick has ceased —
Save for a few.
I walk the floors now lengthened with the night,
Waiting.
So all is quiet for a space.

II

Near overhead, sinking toward the west
Pleiades sparkle, and with Juniper, glowing golden
green,
Mark that hour when fires of life, banked low in
sleep,
So easy flicker out.
A softly speaking nurse directs me to the bed
Where the last ember just winked out
Amid the ashes of a life.

I look at him, who fought my father's War.
Tatoo'd on arm, the Eagle, Globe and Anchor,
With proud boast "Belleau Wood",
Mark a Marine.
(Once one, always one.)
Semper fidelis.

Minenwerfer and Mauser, phosgene and screaming
steel
Spared him, so many years ago.
Death's angel found him not,
Until now.

The open eyes gaze straight ahead, unseeing,
Lustreless, which so many years ago roved
glittering
At Mam'selle and Fraulein, or blinked with fear
Above hunched shoulders and shortened neck,
while mortar shells
Their near-miss muddy benedictions gave.

I listen for the beat of heart,
Two thousand million beats or more now done,
Keeps silence.
I slowly straighten up.
For his soul's respose, a prayer forms on my lips,
Unheard, except by God.

III

'Tis later now; a streak, dull crimson, ribbons the
eastern sky.
What used to be a man lies here.
His yellow skin, with bulging belly, swollen feet,
Tell of wine that maketh glad the hearts of men.
It was too much his friend,
And enemy.
Black-crusted dries the blood upon his lips.
Death, advertising his approach, rattles in his lungs.

Helpless, all remedies now used, I watch,
Wondering that this bloated yellowness has seen
another dawn.
Outside, upon the oak tree's leafless crown
A blue jay rasps greeting to the risen sun,
And life goes on.
Jam orto lucis sidere, Amen.

*Chief, Ophthalmology Section, Surgical Service, Veterans Administration Center, Togus, Maine 04330.

Asymptomatic Pulmonary Nodule

A 25-Year Survey

FENNELL P. TURNER, M.D.*

The cancer potential of an asymptomatic undiagnosed pulmonary nodule has become well recognized during the past 20 years. Of particular interest has been the series of papers published as the result of a ten-year nationwide cooperative study utilizing material from 78 Veterans Administrations and Armed Forces hospitals.[1,2,3,4] Asymptomatic nodules in 1,134 patients had been entered into this study over a five-year period of time. Found to be bronchogenic carcinoma were 392 lesions (32%), and curative surgery was found to be possible in 309 patients or 78.9%.

SELECTION OF CASES AT TOGUS, MAINE

The Surgical Service at the VA Hospital, Togus, Maine, having contributed 12 cases to this cooperative study, has continued to maintain the protocol and has now accumulated a series of 80 consecutive surgically treated patients over a 25-year period of time. These 80 patients were a highly selected group. It has been routine throughout this 25-year period to screen patients with pulmonary disease in a combined Medical-Surgical Chest Conference prior to surgical treatment. Consultants in chest medicine and thoracic surgery from various hospitals throughout the State have attended these conferences and various points of view have been expressed. In some instances immediate surgical treatment was recommended. In some instances close follow-up was the consensus. Several patients were eventually operated upon elsewhere. Other patients were operated upon within a month or two of first observation and as soon as it could be determined that there was growth or as soon as it could be found that there had been no evidence of the existence of the same lesion on admission elsewhere at any time in the past.

Twenty patients with malignant pulmonary "coin" lesions were not included in this survey as they had become symptomatic (pain, cough or hemoptysis) just prior to admission to the hospital. Two others were found to have positive "Pap" smear on sputum immediately prior to operation. Ten patients with operated benign "coin" lesions were omitted from the study as they too had been symptomatic (cough, hemoptysis, pleurisy and/or history of chills and fever). Another six malignant lesions were omitted as on surgical exploration they were found unresectable (three because of mediastinal lymph node involvement, one because of involvement of chest wall and mediastinal pleura, and two because poor pulmonary function would not have permitted a required pneumonectomy). Two patients were omitted as after resection had been completed the pathologist confirmed that the "coin" lesion in actuality was the primary lesion and that a brain lesion in one and mandibular involvement in the other were actually metastatic foci. Finally an estimated 50 to 60 or more "coin" lesions seen in Chest Conference during the same period of time were not operated upon as they were believed to have been quiescent granulomatous lesions which had either shown no growth over a period of years or had been found to have been present in x-rays of the chest during previous hospital admissions, elsewhere in the State or perhaps while in Service.

TABLE 1

RESECTED ASYMPTOMATIC, UNDIAGNOSED SOLITARY PULMONARY NODULES* V.A. HOSPITAL, TOGUS, ME. 1952-1977

Malignant Tumors		55
Squamous Cell Ca	26	
Adenocarcinoma**	15	
Undifferentiated Ca	5	
Adenoma (Carcinoid Type)	2	
Metastatic Tumors (Miscellaneous)	6	
Choriocarcinoma	1	
Benign Lesions		25
Hamartoma	4	
Granuloma (Including tuberculoma)	14	
Infarct, old	1	
Ossification	1	
Fibrosis	1	
Chronic abscess	1	
Bronchogenic cyst	1	
Lipoma	1	
Cyst of pleura	1	

*All histopathology was reviewed by Kenneth E. Smith, M.D. and Danielle Mutty, M.D., Pathologists

**Bronchiolar-alveolar Ca 4 cases

TABLE 2

DISTRIBUTION OF "COIN" LESIONS BY SIZE

	Median Diameter in Cms.
2 Adenoma	1.5
25 Benign	2
6 Metastatic Ca	2.3
15 Adenocarcinoma	3
26 Squamous Cell Ca	3
5 Undifferentiated	4
1 Choriocarcinoma	6
80	

*Chief, Surgical Service, Veterans Administration Center, Togus, Maine 04430.

Supported by the Medical Research Service of the Veterans Administration.

TABLE 3

RESECTED SOLITARY PULMONARY NODULES
COMPARATIVE INCIDENCE OF CANCER IN 4 STUDIES

	Fitzsimmons Army Hosp. 1958		*VA-Armed Forces Coop. Study 1975*		*Garfield Mem. Hosp. (Georgetown U) 1956*		*VAC Togus, Me. 1978*	
	No.	%	No.	%	No.	%	No.	%
Granulomas	183	77.6	474	53.5	83	38.6	14	17.5
Malig. Tumors	23	9.7	316	35.6	101	47	55	68.75
Misc. Benign	30	12.7	97	10.9	31	14.4	11	13.75
Total	236		887		215		80	

TABLE 4

MALIGNANT SOLITARY PULMONARY NODULES
(Distribution by Age)

Age	*15-19*	*20-29*	*30-39*	*40-49*	*50-59*	*60-69*	*70-79*	*Total*
Togus VA			4	3	21	25	2	55
Georgetown U.*		1	12	22	37	22	7	101
Fitzsimmons Army Hospital**		2	5	4	8	3	1	23
Fitzsimmons (Benign Lesions)	4	79	78	40	9	3	0	213

*See Reference 5
**See Reference 6

STATISTICAL RESULTS OF STUDY

Of the 80 consecutive resected, asymptomatic and undiagnosed "coin" lesions, 55 (68.75%) were malignant and 48 of these were primary in the lung (Table 1). The diameter varied from 1.5 cm. to 6 cm. (Table 2). It seems reasonable to have found that the rapidly growing malignant tumors were generally larger in size than the benign lesions. It is generally agreed that adenomas are potentially malignant[7] and may sometimes reach large size. The incidence of malignancy among the patients with resected solitary pulmonary nodules was found to be higher than that generally reported (Table 3 and 4). This is probably so for the following reasons: few active duty personnel, fewer young veterans as patients than 15 and 20 years ago, a lesser incidence of histoplasmosis and coccidioidomycosis than would be found in hospitals in the central and western states and finally a decrease in recent years in pulmonary tuberculosis. Operations carried out in these 80 patients are listed in Table 5. A greater number of wedge resections and simple excisions were carried out in patients with benign disease. Our postoperative mortality was 3.75% (Table 6).

There were 55 malignant tumors and 48 of these were primarily pulmonary in origin. There were six solitary pulmonary metastases from malignant lesions in other organs. One patient lived 14 years after resection of adenocarcinoma of the sigmoid colon and 12 years and 6 months after resection of a solitary pulmonary metastasis from this tumor. Death was not related to his cancer. Four other patients with metastases from melanoma, fibrosarcoma, kidney and bladder were all dead of their disease within three years. One patient with a metastasis from the embryonal cell carcinoma of the testis is now on chemotherapy without evidence of recurrence after two years. Finally the patient with the choriocarcinoma died two years and nine months after operation, of a massive CVA with hemiparesis. He was 69 years old.

TABLE 5

SOLITARY ASYMPTOMATIC UNDIAGNOSED PULMONARY NODULES
OPERATIVE PROCEDURE IN 80 CONSECUTIVE PATIENTS

Procedure	*Benign Nodules*	*Malignant Nodules*	*Total*
Pneumonectomy	2	6	8
Lobectomy Plus	0	7	7
Lobectomy	9	34	43
Segmental	5	5	10
Wedge	7	3	10
Excision	2	0	2

TABLE 6

SOLITARY ASYMPTOMATIC PULMONARY NODULES
OPERATIVE COMPLICATIONS IN 80 CONSECUTIVE PATIENTS

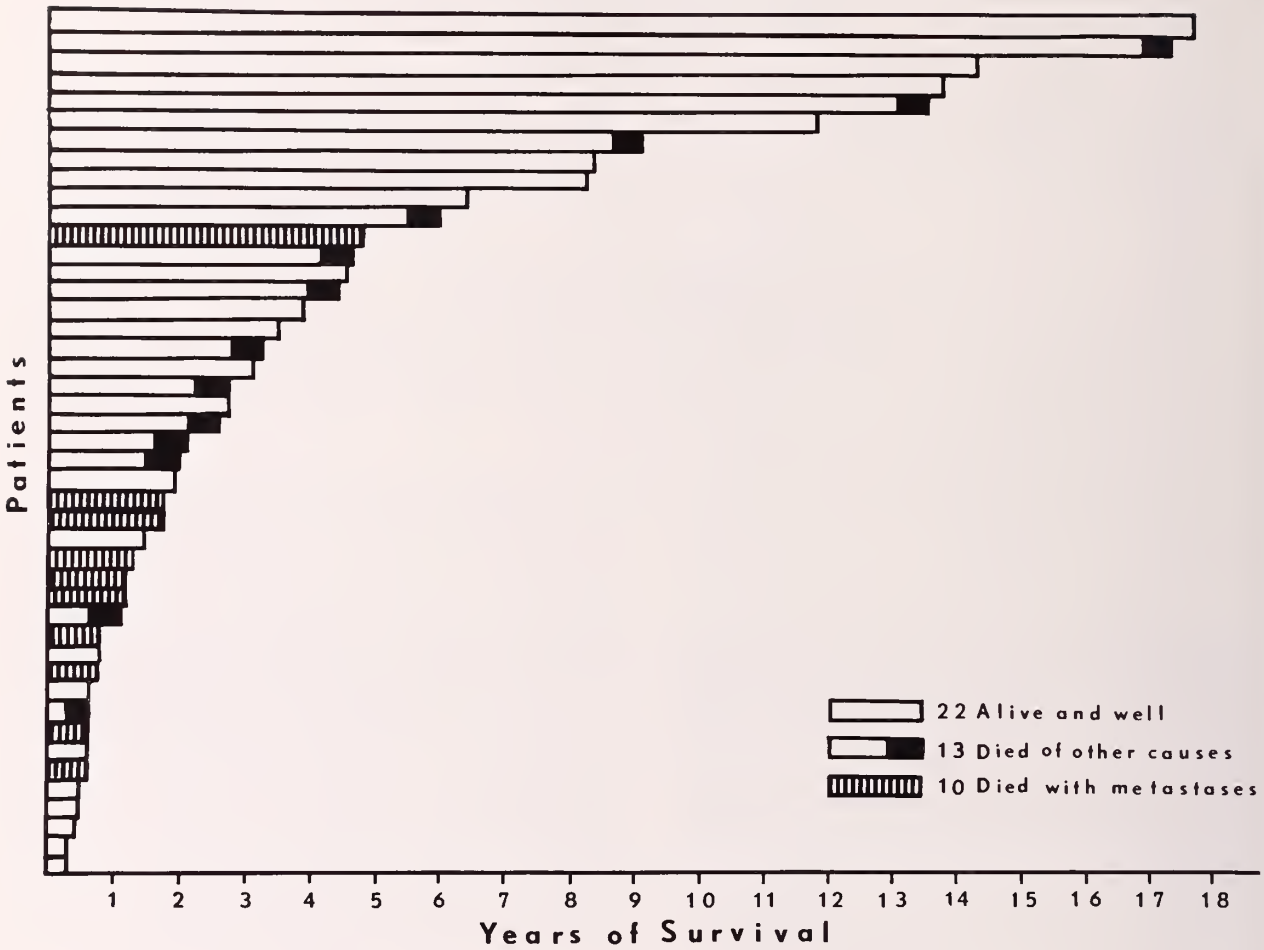
*Cardiac arrest	1	
*Acute M.I.	1	
Atrial fibrillation	4	
Acute cardiac decompensation		
Atelectasis and/or pneumonia	3	
Persistent pneumothorax	3	
*Staphylococcal pneumonia	1	
Acute cholecystitis	1	
Acute brain syndrome	1	
Thrombophlebitis	1	
	16	(20%)
*Post-operative deaths	3	(3.75%)

PRIMARY LUNG CANCER

Three of the 48 patients with primary lung cancer died of postoperative complications. The remaining

Table 7

Resected Asymptomatic Solitary Malignant Nodules 45 Consecutive Cases - Survival in Years



45 patients have been closely followed (Table 7). Ten or 22.2% of the patients have died of their disease. All but one of the deaths took place within two years of the time of their operation. At the five-year level, 11 of 26 patients or 42.3% were still living and at the ten-year follow-up level, 6 of 19 or 31.6% were still living (Table 8). If the three patients with oat cell lesions, which have notorious poor survival statistics, are omitted from this series, the five- and ten-year survival values would be 47.8% and 35.3%. Of the 13 patients who died of other causes, three died of primary cancer of a different organ, six other patients also had second cancers (adenocarcinoma prostate, two; seminoma of testicle, one; adenocarcinoma of sigmoid colon, one; epidermoid carcinoma larynx, two). The incidence therefore of a second malignancy in this group of patients with primary lung cancer was 9/48 or 18.75%.

Steele and Buell[3] were able to use data collected from the cooperative study to study the growth rate in 67 different patients. They found that the tumor volume doubling time varied from 30 to more than 300 days (Table 9). They also observed that cellular growth of varying rapidity was observed with all histological types of tumor although it was apparent that rapid growth was more characteristic of the undifferentiated tumor or poorly differentiated epidermoid tumor than it was of any other variety. To use Collins' example[8] if lung cancer cells with an average diameter of ten microns grow at a fixed rate,

Table 8

48 Patients With Asymptomatic Bronchogenic Ca (Follow-Up in 45 Post-Operative Survivors)

	10-Year Survival (6 of 19) 31.6	
	5-Year Survival (11 of 26) 42.3	
10	Patients known to have died with metastases 10/45	22.2%
1	Patient died of a new bronchogenic carcinoma (13 years and 7 months after the 1st operation)	
1	Patient died of epidermoid carcinoma of the esophagus	
1	Patient died of adenocarcinoma of the common duct	
10	Patients have died of other causes (without known evidence of recurrent cancer)	
22	Patients presently living without disease 22/45 (3 months P.O. — 17 years and 8 months P.O.)	48.9%
45	TOTAL	

Table 9

Doubling Time and Cell Type*

Doubling Time (days)	*Sq. Cell*	*Undiff.*	*Adenoca.*	*Bronch.*	*Adenosq.*
30- 60	3	7	1	—	—
61-120	6	11	7	—	—
121-180	5	4	4	1	2
181-240	1	—	4	1	—
241-300	1	1	2	1	—
>300	—	—	3	1	1
Totals	16	23	21	4	3

*Steele and Buell (J. Thorac. and Cardiovasc. Surg., 1973)

20 volume doublings would be required to produce a tumor mass 1 mm. in diameter and 30 doublings to produce a mass 1 cm. in diameter. If tumor doubling were then to continue in exponential fashion with only ten more doublings the tumor mass would now be 10 cm. in diameter and would weigh more than two pounds.

Some rapidly growing tumors will metastasize early. Other lung tumors will grow to large size without evidence of distant spread. Regardless of cell type, however, many peripheral lung tumors can be removed surgically with long-term cure. As a case in point, after "clinical staging" of the 45 operated patients with bronchogenic carcinoma we find that all 13 of the T1 NO MO* lung lesions have had long survival and that none of them have died with metastatic disease (Table 10). On the other hand, 6 of the 26 (23%) T2 NO MO lesions died of metastatic disease and four of the six (67%) lesions that showed regional lymph node involvement have also died of metastatic disease.

Table 10

Solitary, Asymptomatic, Undiagnosed, Pulmonary Nodules Clinical Staging in 45 Patients With Primary Lung Cancer

Stage	*Patients*	*Alive*	*Dead of Cancer*	*Dead of Other Causes*
T1 NO MO	13	10	0	3
T1 N1 MO	4*	1	2	1
T2 NO MO	26	11	6	9
T2 N1 MO	2*	0	2	0
Total	45			

*6 Patients with positive regional nodes, 4 dead with cancer (67%)

Table 11

Solitary Pulmonary Nodule Surveys Incidence of Cancer

		Percent
Mass Surveys of General Population		3- 6
8 Retrospective Hospital Studies (1953-1961)		10-68
Fitzsimmons General Hospital (1958)	Total	10
(U.S. Army Hospital — Denver)	Under Age 50	5
	Over Age 50	50
USVA-Armed Forces Coop. Study (1963)	Total	35
	Under Age 50	15
	Over Age 50	56
VA Togus, Maine (1977)	Total	69
	Under Age 50	37
	Over Age 50	80

Discussion

In this survey we have confirmed the findings of others, including the cooperative VA-Armed Forces study by 78 hospitals that asymptomatic pulmonary nodules are sometimes found to be malignant even in young adults but are proportionately more common in men over the age of 40. In all men over the age of 50, the chance of an asymptomatic pulmonary nodule being malignant is from 50 to 80% depending on the type of hospital population (Table 11).

We have found also that after removal of a T1 NO MO tumor the chance of long survival is much greater than after the removal of solitary lung tumors of greater size or of more extensive disease (T2) or of those that have regional lymph node involvement (T1 N1 MO or T2 N1 MO) and we have even found that it is possible to follow a resected lung cancer patient for as long as 13 and one-half years, during which time the patient remained a confirmed, heavy, habituated cigarette smoker, only to find out that the patient had now developed a new primary lung cancer on the other side for which no therapy was of any value.

The question will be asked, "How can we best control this epidemic of primary bronchogenic carcinoma?" Prevention first comes to mind. The part that tobacco smoke, automobile exhaust, factory fumes, and industrial wastes plays in the etiology of lung cancer has been extensively studied and much more work needs to be done. In the meantime, mass roentgenographic surveys of men and women who are at risk should be encouraged. Tobacco users and workers in certain industries who are over the age of 40 should have yearly chest x-rays whereas heavy smokers over the age of 50 should be advised to have x-rays every four to six months. Oblique and apical lordotic views are useful in visualizing lesions in some hard to reach locations. Tomography should be carried out whenever doubt arises about some of the softer shadows. Sputum samples should also be collected for "Pap" smears from certain high risk

*T1 NO MO pulmonary lesions are defined as tumors with a diameter less than 3 cm. and without positive lymph nodes or evidence of distant metastases.

individuals. The discovery and excision of small asymptomatic malignant nodules is said to represent no more than five or ten percent of the patients with lung cancer. However, with earlier discovery of the small peripheral lesions perhaps the percentage of the total lung cancer population that this entity represents will be doubled.

At this point it is useful to remember that in the Cooperative Study 26% of the patients had been followed for from 6-48 months before operation. This is far too long. Six of the ten patients in the survey just presented who had died because of their lung cancer had lesions when operated upon 3 cm. in diameter or larger. Earlier discovery and earlier treatment might well have resulted in cure in these patients. Three of the other four patients had been followed for at least 11 months before being referred to surgery. Prolonged watching and waiting has been advocated in the past. We are of the opinion that any small lesion that is known to have recently developed and particularly those that have irregular, fuzzy or notched borders should be removed with little delay. Well intended procrastination and prolonged waiting should not be indulged in. It is true that some lung cancers will grow slowly over a period of many months but we believe that any growth at all demands removal. Neither is an extensive pre-operative study indicated in the asymptomatic patient with a small peripheral lesion. The yield from such investigation is very small and besides it is expensive and time consuming. Removal is necessary in order to establish diagnosis. It is critical that the cancer be excised before cells have a chance to spread into the perivascular lymphatics and before it has an opportunity to invade thin walled veins and shed cells into the blood stream.

Now what happens if small lung cancers are not removed? Would these patients live as long as those who had been surgically treated? A record was kept of thirteen such patients who had come to my attention during this 25-year period. All of these patients died of their disease without having definitive therapy and all were patients who had been found to have a solitary asymptomatic peripheral lung nodule and who for various reasons: age, infirmity due to other severe illness, chronic brain syndrome, chronic obstructive lung disease or lack of informed consent from patient or from guardian, etc. had neither been operated upon nor had they received definitive cancer therapy. In this group, eventual demise took place in from one month to five years and six months with a mean survival of two years and one month. Four patients were found to have squamous cell carcinoma, three had adenocarcinoma and two had undifferentiated carcinoma. In four patients, autopsy examination was not carried out. Of the nine who had autopsies, six were found to have widespread metastases: the other three showed extensive local growth, one with hilar

Continued on Page 192

Tablets
Percocet®-5 CII

DESCRIPTION Each tablet of PERCOCET®-5 contains 5mg oxycodone hydrochloride (WARNING: May be habit forming), 325mg acetaminophen (APAP).

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone or acetaminophen.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCOCET®-5, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCOCET®-5 is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCOCET®-5 should be cautioned accordingly.

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCOCET®-5 may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCOCET®-5 should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCOCET®-5 should not be administered to children.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions The administration of PERCOCET®-5 or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients PERCOCET®-5 should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. PERCOCET®-5 is given orally. The usual adult dose is one tablet every 6 hours as needed for pain.

DRUG INTERACTIONS The CNS depressant effects of PERCOCET®-5 may be additive with that of other CNS depressants. See WARNINGS.

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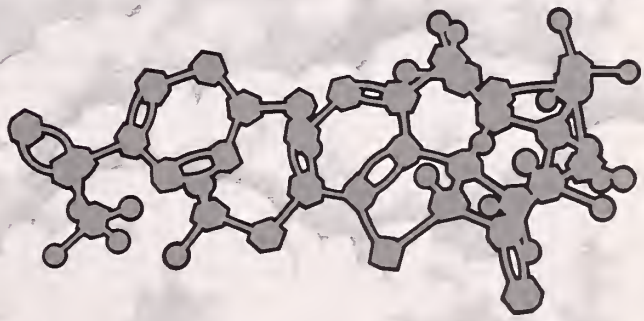

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Please see facing page for Brief Summary of prescribing information.

lymph node metastases and one with a solitary 1.5 cm. liver metastasis. In two patients there was terminal GI hemorrhage from gastric ulceration.

So here we have 13 patients with untreated solitary malignant pulmonary nodules with 100% mortality within five and one-half years, to be compared with 48 patients with surgically treated malignant nodules where there was a 54% mortality (26 patients) from all causes, with several survivors who have now been followed for more than 17 years. In actuality only ten patients of the 45 postoperative survivors are known to have died of their disease.

Conclusions

1. A 25-year study of asymptomatic solitary pulmonary nodules once again has indicated that the incidence of malignancy amongst these nodules is high and that it increases rapidly with the increasing age of the patient population.

2. If there is (a) no spread of cancer to adjacent pulmonary segments, (b) no involvement of pleural surfaces, (c) no involvement of regional lymphatics and hilar lymph nodes, and (d) if the mass is less than 3 cm. in diameter, following resection long survival will ensue.

3. An aggressive surgical approach is advocated in the management of all solitary pulmonary nodules found in patients at high risk, particularly heavy cigarette smokers over the age of 40.

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Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The Maine Medical Association's House of Delegates, at its June 1976 meeting, adopted a regulation stating that a *minimum of 150* hours of continuing medical education is required in order to maintain membership. The policy took effect on January 1, 1977 and all members must be certified by January 1, 1980. Eligibility for certification begins January 1, 1977.

Credits required for the three-year period are as follows:

Category 1 — CME Activities with Accredited Sponsorship **(60 hours required)**	**No limit**
Category 2 — CME Activities with Non-accredited Sponsorship	**45 hours**
Category 3 — Medical Teaching	**45 hours**
Category 4 — Papers, Publications, Book and Exhibits	**40 hours**
Category 5 — Non-supervised individual CME Activities	**45 hours**
Category 6 — Other Meritorious Learning Experience	**45 hours**

Only active, dues-paying members are required to report. Please fill in your activity report promptly and return to the M.M.A. office, P. O. Box 250, Brunswick, Maine 04011.

Self-Help in Mental Health?

Impressions of Recovery, Inc.

DANA M. SHELDON, M.D.*

As a practicing eclectic general psychiatrist, the author has been concerned especially with prevention of recurrent emotional and mental illness. This article outlines his experience from 1961-1977 with referrals of patients to Recovery, Inc., a self-help group active since 1938.

Recovery, Inc. was founded by Abraham A. Low, M.D., Associate Professor of Psychiatry and Neurology, University of Illinois, a remarkable pioneer in psychiatry. He worked in the Illinois State hospital system and in 1932 was appointed Assistant State Alienist. He was concerned with the care of patients discharged from the State mental hospitals, and started experimenting with groups of patients. He and the patients evolved the Recovery method by trial and error over several years, the goal being lasting rehabilitation conducted by patients themselves. Dr. Low wrote a book outlining the method.[1] He believed that no case was hopeless and that patients could learn how to cope with emotions and control their actions. His book explains and demystifies symptomatology in a commonsense manner. It outlines the means patients can use to develop control over symptoms and ultimately to eliminate many of them. Any patient can identify with symptoms described in the book. The book embodied the best current thinking on rehabilitation methods and was far ahead of its time.

By 1952, several groups had spread out from Chicago and all functioned without professional supervision. Dr. Low died in 1954 but his organization continued to grow. In 1975, there were 1,000 groups with 15,000 members in the United States, Canada and Puerto Rico. Beginning in 1969, panel discussions of Recovery have been held at the annual meetings of the American Psychiatric Association. Although Dr. Low encountered much skepticism from colleagues during the analytically dominated years of American psychiatry, in recent times several prominent mental health professionals have endorsed Recovery, Inc.

The Recovery headquarters in Chicago is staffed by about seven paid members. It is a non-profit, non-sectarian organization supported by voluntary contributions and optional paid memberships. At a meeting members contribute what they can afford, often fifty cents or less. All money collected is used to pay for transporting leaders-in-training, for the few staff salaries, correspondence, etc. Expenses are very minimal. Members need purchase only Dr. Low's book for approximately eight dollars if they so desire.

The nation is divided into districts, each one supervised by a volunteer leader. The leader meets regularly with group leaders in his district for supervision and training. Forty-seven states have Recovery groups, the exceptions being South Carolina, Hawaii and Vermont. There are 10 groups in Puerto Rico, dozens in 8 provinces of Canada, and 10 in Ireland. A directory is available from headquarters listing the place and time of all meetings and the leader's telephone number. Many large cities list Recovery in the telephone book and an answering service will give information about local meeting times. In the greater Boston area, for example, there are 15 meetings.

Meetings usually occur weekly in a public, nonprofessional setting — library, church, YMCA, etc. They are open to anyone aged eighteen or older. Most meetings begin at 7:30 or 8:00 p.m. but some take place in the morning or afternoon. They last one and one-half to two hours. Professionals are welcome as observers and may ask questions *after* the meeting. Proceedings begin with the leader informally welcoming new members. A passage from Dr. Low's book may then be read aloud by members, or a tape of Dr. Low's may be played describing some aspect of his method. Volunteers then present "an example" in a previously defined format. They describe an event — time, place and how they reacted — then symptoms and discomfort are described. They then "spot," i.e., describe their insight into the episode and their reaction, insight gained from learning the method. Lastly, they describe how they would have reacted before coming to Recovery. The "example" should be a trivial, everyday event and the leader specifically avoids unusual or non-trivial events. Dr. Low believed that if one can learn to cope with trivial situations in an adaptive manner, the same principles would carry over to complex situations.

After the presenter finishes, the leader recognizes members who wish to "spot" on the example and offer additional insights. These may be supportive or may illuminate the personal dynamics of the presenter. Each example requires about fifteen minutes and three or four are presented at a meeting. After all the examples have been given, five to ten minutes is reserved for questions and comments, then an informal "mutual-aid" period of small group discussions takes place. Refreshments may be served. Conversation is guided by Recovery principles. This is an invaluable opportunity for new members

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to question older members and is a fine source of hope.

Recovery emphasizes self-leadership; that is, taking responsibility for oneself. It does not foster dependency and within a group members feel a nice balance between empathy, caring, encouragement, acceptance and a non-judgmental atmosphere. I have never seen a patient nor heard of one who was harmed by Recovery. The groups discourage charity and do not encourage socializing, although a little does occur and is acceptable. Members may call another member during a crisis and talk for as long as five minutes, during which time some "spotting" often occurs. Members do not diagnose or discuss medications but they do encourage one another to follow the advice of psychiatrists and other professionals. Recovery, though not formally linked to mental health agencies, is anxious to cooperate with them and shows none of the anti-professional attitudes evident in some self-help groups. Recovery members often hold a typical meeting or panel to demonstrate the method to professionals. The author has, in the past sixteen years, referred perhaps three hundred patients to Recovery groups from private practice, community mental health centers, State mental hospitals and a Veterans Administration hospital. A mistake was made early by not referring above-average intelligence patients until some went on their own, to the education of the author. Many of the patients continued in treatment with the author while others were able to do well with Recovery alone. An effort was made to shift patients toward Recovery whenever appropriate. As soon as rapport was established, a referral would be suggested, the patient's defenses would be analyzed, and he was encouraged to attend five meetings before making a commitment. Some patients leap at the opportunity on the first visit, others require a year or more before they will try a meeting. It is important for the therapist to discuss with them the fears, projections and rationalizations which they had while attending the initial meetings. One patient with a paranoid schizophrenic reaction, multiple phobias and severe obsessive characteristics had dutifully sat in psychiatrists' offices for twenty years. He was waiting for them to "cure" him. After his second Recovery meeting he had an acute anxiety attack when he realized that he was expected to "cure" himself and felt totally unable to do so. With encouragement he persevered, became a very faithfully attending member and slowly but surely improved over the next two years.

Patients should attend meetings once or twice weekly, read the book regularly, and practice the method — all three are important. Results may occur rapidly or slowly, but if patients work at it, all get results. It takes most patients about one year of weekly meetings before they have a good grasp of the method and can practice it efficiently. Some become very adept at "trigger spotting," or developing very rapid insights when symptoms begin. This may enable them to shorten the symptomatic period dramatically. Whereas an anxiety attack previously may have produced symptoms for days, they may be shortened to a few hours or minutes.

It is helpful if the referring physician, with the patient's permission, will call the group leader before the first meeting. If, for instance, the patient is unable to speak in the meeting, the leader will be forewarned. Leaders are not obligated to report back to a physician on a member's conduct, although Recovery reminds members "to follow the doctor's authority."

Which patients are suitable for referral? Anyone eighteen or older who can sit quietly for an hour at a meeting and who doesn't have severe memory defects or retardation problems. The ability to read is important. Patients with anxiety usually respond faster than those with depression but the latter will ultimately gain a great deal if they continue to attend meetings. If the referring person believes in the effectiveness of Recovery and supports the patient, after several months to a year the patient will almost certainly report that Recovery is worthwhile and is "working" for him. Frequently, patients who have had multiple psychiatric or medical admissions are able to decrease or eliminate psychotropic medications and avoid rehospitalization. Some patients need to continue in Recovery for many years while others feel able to quit after one or more years, perhaps returning for a time if symptoms recur. Attendance promotes growth and independence, not regression and support-seeking behavior. In fact, patients who are not willing to work at the Recovery method often do not really want self-help, preferring to lean on others.

An excellent study of 500 Recovery groups including 6,463 members was reported by Hanus Grosz, M.D. in 1972 and 1973.[2,3] Questionnaires were filled out by 97% of those attending. Fifty-two percent of the members had been hospitalized before joining Recovery and only twelve percent since attending meetings. Forty-nine percent of the members had been attending meetings for more than one year, most of them about once a week. Seventy-eight percent of the relatives of members approved of Recovery and four percent disapproved.

In April 1977, six Recovery members conducted a demonstration panel at Togus, Maine under the auspices of the Cooperative Health Education Program of the Veterans Administration. This meeting gave enough impetus so that Recovery, Inc. came to Maine in December 1977, starting a group in Brunswick on Sunday afternoons. Meetings are now held in South Portland on Saturday mornings. It is open to the public., i.e., to those of age 18 or older. Professionals are welcome to observe. Further information is available from Recovery, Inc., 116 South Michigan Ave., Chicago, IL 60603 or from P.O. Box 3156, Togus, Maine 04330. It is hoped that additional meetings will develop

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108th Legislature — 2nd Regular Session

Summary

JOHN R. MCKERNAN, JR., Esquire*

The Maine Legislature adjourned *sine die* on April 6, 1978. This is a review of each Legislative Document with which the Maine Medical Association was involved during the session.

1. L.D. 1948 — AN ACT to Provide for Reform of the State Tax Laws, Including the State Sales Tax and State Income Tax (Compromise bill supported by Governor).

   M.M.A. Objective: Support the legislation so long as it includes a reduction in the personal income tax.

   Result: Objective accomplished. Amended version enacted. Chapter 686 of the Public Laws.

2. L.D. 1958 — AN ACT Relating to Post-Graduate Education in the Field of Medicine, Dentistry, Optometry and Veterinary Medicine (redraft — L.D. 2177).

   M.M.A. Objective: Eliminate the 80% payback requirement for "Compact" students who return to practice in Maine.

   Result: Objective partially accomplished. New draft enacted allowing for forgiveness of the student's state capitation payment so long as he or she practices for a specified length of time "in primary care or other specialized areas as determined by the Commissioner with the advice of the Advisory Committee on Medical Education." Chapter 703 of the Public Laws.

3. L.D. 1968 — AN ACT to Reorganize Certain Boards and Commissions and to Affiliate Certain Boards and Commissions with Departments of Maine State Government.

   M.M.A. Objective: Delete the provision in the legislation which required the Board of Registration in Medicine to channel its budget through the Department of Human Services to the Governor.

   Result: Objective not accomplished. Provision retained in the amended version enacted. Chapter 604 of the Public Laws.

4. L.D. 1975 — AN ACT Concerning Substitution of Generic Drugs by Pharmacists.

   M.M.A. Objective: Maintain the provision in the current law allowing a checkoff box for substitution of generic drugs.

   Result: Objective accomplished. Amended version enacted. Chapter 611 of the Public Laws.

5. L.D. 1993 — AN ACT Appropriating Funds to the Grant-Loan Scholarship Fund for Physicians at the New England College of Osteopathic Medicine.

   M.M.A. Objective: Monitor legislation to make sure that if the additional positions are funded, the scholarship fund be eliminated.

   Result: Objective accomplished. Bill withdrawn, and provisions M.M.A. supported included in L.D. 2177, c.703 of the Public Laws.

6. L.D. 1997 — AN ACT Amending the Maine Medical and Hospital Malpractice Joint Underwriting Association Act.

   M.M.A. Objective: Support passage of the legislation in order to aid in the formation of a physician-owned malpractice insurance company.

   Result: Objective accomplished. Amended version enacted. Chapter 643 of the Public Laws.

7. L.D. 2013 — AN ACT Relating to Certificate of Need.

   M.M.A. Objective: Support limiting the legislation to the minimum federal requirements, which would not include physicians' offices within the Certificate of Need Program.

   Result: Objective accomplished. Amended version enacted. Chapter 687 of the Public Laws.

8. L.D. 2021 — AN ACT Adjusting Appropriations and Allocations for the Expenditures of State Government and Changing Certain Provisions of the Law Necessary to the Proper Operations of State Government for The Fiscal Years Ending June 30, 1978 and June 30, 1979. (redraft — L.D. 2195).

   M.M.A. Objective: Support legislation including increase in funding for the Office of the State Medical Examiner, increasing funding for psychiatrists at State institutions, and repeal of the 10% reduction language in last year's Medicaid budget.

   Result: Objective accomplished. Amended version, including all of our provisions, enacted. Chapter 712 of the Public Laws.

9. L.D. 2042 — AN ACT to Clarify Statutes Relating to the Confidentiality of the Records of the Department of Mental Health and Corrections.

   M.M.A. Objective: Insure that if legislation passes, it does not jeopardize peer review records.

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Result: Objective accomplished. Bill withdrawn.

10. L.D. 2051 — AN ACT to Lower the Cost of Medical Malpractice Arbitration.
    M.M.A. Objective: Insure that the panel of three arbitrators in medical malpractice cases is maintained.
    Result: Objective accomplished. Amended version enacted. Chapter 662 of the Public Laws.
11. L.D. 2055 — AN ACT to Provide a $250,000 Grant to the New England College of Osteopathic Medicine.
    M.M.A. Objective: Monitor legislation.
    Result: Objective accomplished. Bill became law despite the Governor's veto. Chapter 715 of the Public Laws.
12. L.D. 2065 — AN ACT to Amend the Child Welfare Laws.
    M.M.A. Objective: Monitor legislation and offer amendment to provide immunity for physicians who render emergency medical treatment to minors under the Department of Human Services Program.
    Result: Objective accomplished. Amended version enacted. Chapter 644 of the Public Laws.
13. L.D. 2067 — AN ACT to Clarify the Rights and Responsibilities of Institutions to Provide Medical Care.
    M.M.A. Objective: Monitor legislation to insure that if passed, a physician could order administration of prescription medication orally as well as by written order.
    Result: Objective accomplished. Bill withdrawn.
14. L.D. 2078 — AN ACT to Clarify Procedures for Emergency Admission to Hospitals for Mentally Ill.
    M.M.A. Objective: Support passage.
    Result: Objective accomplished. Amended version enacted. Chapter 629 of the Public Laws.
15. L.D. 2136 — AN ACT to Establish the Health Facilities Information Disclosure Act.
    M.M.A. Objective: Insure confidentiality of treating physicians in information which is submitted to the Health Facilities Cost Review Board.
    Result: Objective accomplished. Amended version enacted. Chapter 691 of the Public Laws.
16. L.D. 2183 — AN ACT to Provide for Reform of the State Tax Laws (Republican-sponsored plan).
    M.M.A. Objective: Secure passage of legislation including a reduction in personal income tax rates.
    Result: Objective partially accomplished. Bill defeated, but income tax provisions were enacted as part of L.D. 1948, c.686 of the Public Laws.
17. L.D. 2184 — AN ACT to Provide for Reform of the State Tax Laws (Democrat-sponsored plan).
    M.M.A. Objective: Defeat legislation.
    Result: Objective accomplished. Bill Defeated.

Other Public Laws enacted this session which may be of interest are:

L.D. 2024 — AN ACT to Empower Administrative Hearing Officers to Sign Fair Hearing Decisions. Chapter 594 of the Public Laws.

L.D. 1905 — AN ACT to Enable the Purchase and Administering of Barbiturates for the Euthanasia of Pets and Animals. Chapter 609 of the Public Laws.

L.D. 1938 — AN ACT Establishing Vision Test Requirements for Driver License Renewals. Chapter 620 of the Public Laws.

L.D. 2064 — AN ACT to Provide for Limited Guardianship. Chapter 627 of the Public Laws.

L.D. 2091 — AN ACT to Clarify Admission Procedures at Pineland Center. Chapter 635 of the Public Laws.

L.D. 1974 — AN ACT to Allow Nursing Homes to Provide Physical and Occupational Therapy to Residents in Need of that Care. Chapter 646 of the Public Laws.

L.D. 2150 — AN ACT to Encourage Early Resolution of Discrimination Complaints and to Clarify the Subpoena Power of the Maine Human Rights Commission. Chapter 648 of the Public Laws.

L.D. 2160 — AN ACT Providing for Notice to Parents Under the Child Abuse and Neglect Statutes. Chapter 652 of the Public Laws.

L.D. 2016 — AN ACT Relating to the State Board of Social Worker Registration. Chaptr 673 of the Public Laws.

L.D. 2111 — AN ACT to Establish and Apply a Policy on the Classification of Major Policy-Influencing Positions Below the Head of State Department and Agencies. c.674 of Public Laws.

L.D. 2085 — AN ACT to Abolish the Health and Mental Retardation Improvement Fund and Make Provision for Future Funding of Existing Programs Under the General Fund. Chapter 680 of the Public Laws.

L.D. 2189 — AN ACT to Revise the Maine Sunset Law and State Agency Rules Law. Chapter 683 of the Public Laws.

L.D. 2190 — AN ACT Relating to the Place of Filing Under the Uniform Commercial Code. Chapter 702 of the Public Laws.

L.D. 2005 — AN ACT to Provide Funding for Programs to Aid School Administrative Units to Identify and Provide Special Educational Programs for Gifted and Talented Children.

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MAC and Maine's Generic Substitution Law

JOHN R. MCKERNAN, JR., ESQUIRE*

What is MAC? MAC is an acronym for "Maximum Allowable Cost," the limitation established by the national Pharmaceutical Reimbursement Board for reimbursement to pharmacists under Title XIX of the Social Security Act for certain designated prescription drugs. Under the MAC program, the maximum allowable reimbursement for a drug product is "the lowest unit price at which the drug is widely and consistently available from any formulator or labeler." No pharmacist may be reimbursed under Medicaid more than the MAC for any drug on which the Pharmaceutical Reimbursement board has established a MAC unless a physician certifies the medical need for a specific drug product. Thus, if a physician does not certify the need for the brand name on the prescription, the pharmacist will be reimbursed under Medicaid at the MAC rate, so he must substitute a generically equivalent drug or absorb the difference between the cost of the brand name product and the MAC rate of reimbursement.

Compounding the problem for the physician and the pharmacist is the policy of the Department of Health Education and Welfare for physician certification of the need for brand name drugs. Excerpts from the HEW Statement of Policy, outlined in the *Federal Register*, August 15, 1975, Page 34517, include the following:

> Although physicians should not be forced to "justify" the prescribing, it is necessary to have certification of the need for a specific brand name drug in order to achieve the purpose of the policy and to enable the states to monitor its implementation.
>
> The method of certification has been left largely to the states, since Medicaid programs vary in specific administration procedures from state to state. . . .
>
> *A procedure for checking a box on a form will not constitute an acceptable certification since there must be evidence that a physician has made a determination in each case. . . .*
>
> There is only a requirement for certification by the prescribing physician of the necessity for a specific brand in the physician's medical judgment. . . . An example of an acceptable certification would be the notation "brand necessary."(emphasis added)

These guidelines were published in August 1975, and were implemented with the issuance of a MAC on ampicillin on June 27, 1977.†

Since the HEW guidelines on MAC were adopted, numerous states have enacted "generic substitution" laws, and many (including Maine) do not satisfy the HEW requirements for the MAC program. Twelve states have enacted legislation using the two line signature prescribing form.** The two line signature form has at the bottom of the Rx forms two lines as follows:

_____	and	_____
Substitution Permissible		Dispense as Written

The physician is required by state law to sign one of the two lines to validate the drug order.

Maine, since January 1, 1976, has required that all written prescriptions contain a box in the lower right hand corner of the Rx form. Pharmacists may substitute a generic or chemically equivalent drug for the drug specified in the prescription "provided that the substituted drug is listed in the current edition of either the National Formulary or the United States Pharmacopoeia and that the price of the substituted drug does not exceed the price of the drug specified by the prescribing physician" unless there is a checkmark in the box on the prescription form.***

During the most recently completed session of the Maine Legislature, legislation was introduced to conform Maine's law to HEW regulations for the MAC program by requiring physicians to write "this brand medically necessary" on written prescription forms in order to prevent a pharmacist from substituting a generically equivalent drug. The Maine Medical Association opposed the legislation on the basis that the American Medical Association and the Pharmaceutical Manufacturers Association are attempting to change the regulations promulgated by HEW, which do not accept the checking of a box on a prescription form as an acceptable certification of the need for a brand name drug product. Largely due to the arguments advanced by the MMA, the Legislature deleted the provision abolishing the box from the prescription form and passed an amended revision of the original legislation. *The new law, which takes effect July 6, 1978*, changes the existing law only in that it deletes the requirement to the present law that "generically equivalent drug products" be listed in the National Formulary or the United States Phar-

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†Effective April 10, 1978, MAC's were established for tetracycline HCL capsules, propoxyphene HCL capsules, propoxyphene HCL with APC capsules and chlordiazepoxide capsules, pursuant to 42 CFR 450.30 (b) (ii).

**Alaska, Delaware, Georgia, Illinois, Massachusetts, New Jersey, New York, Pennsylvania, Rhode Island, Tennessee, Virginia, Washington.

***32 M.R.S.A. §2806, as enacted by Chapter 476, §1 of the Public Laws of 1975

macopoeia before they may be substituted for brand name drugs.**** The new law maintains the provision that no substitution is permitted if the prescribing physician checks the box on the prescription form.

What the discrepancy between Maine law and federal regulations means to physicians and pharmacists is important. A pharmacist will be reimbursed under Title XIX, the MAC listed by the Pharmaceutical Reimbursement Board on certain drugs unless the physician has, in his own handwriting, written "brand necessary," or some equivalent statement. If a physician checks the box on his prescription blank, a pharmacist is prohibited under Maine law from substituting a generically equivalent drug, yet under the federal regulations if the person for whom the prescription is written is a Medicaid recipient, the pharmacist can legally be reimbursed only the MAC price, which is based on a generic equivalent. Therefore, the pharmacist has the option either of filling the prescription at a loss or contacting the physician to rewrite the prescription.

The unfairness to pharmacists of the discrepancy between Maine and federal law is obvious. Therefore, if the federal regulation are not changed during the next six months to allow the "box/checkoff" approach to certification under the MAC program, there will undoubtedly be legislation introduced during the next session of the Maine Legislature conforming Maine's law on generic substitution to the federal requirements. It will be difficult for the M.M.A. to justify opposing such a change if we have been unsuccessful at the federal level in having our state law deemed acceptable under the federal regulations for the MAC program, especially since every indication is that in the next couple of years, there will be between forty and fifty drugs subject to the MAC limitations.

****32 M.R.S.A. §2806 as enacted by Chapter 611 of the Public Laws of 1977.

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throughout the State whenever leaders can be trained.

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3. Grosz, H.J.: Recovery, Inc. Survey, Second Report, Chicago: Recovery, Inc., May 1973.

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Chapter 706 of the Public Laws.

L.D. 1952 — AN ACT to Increase the Reimbursement for Small Size Boarding Homes and Adult Foster Homes. Chapter 708 of the Public Laws.

L.D. 1972 — AN ACT Concerning the Catastrophic Illness and Medically Needy Program. Chapter 714 of the Public Laws.

L.D. 1973 — AN ACT to Expand the Elderly Low-Cost Drug Program. Chapter 718 of the Public Laws.

L.D. 1976 — AN ACT to Allow Intermediate Care Facilitated to be Reimbursed Under the Medically Needy Program. Chapter 719 of the Public Laws.

Unless the Laws are labeled "Emergency", they will become effective on July 6, 1978. If they are "Emergency" Laws, they are already in effect.

Russell R. Miller, Pharm.D., Ph.D.
and David J. Greenblatt, M.D., Editors

Drug Therapy of Status Epilepticus

THOMAS R. BROWNE, M.D.

ABSTRACT

In managing tonic-clonic status epilepticus one should: (1) maintain vital functions at all times, (2) identify and treat precipitating factors, and (3) administer an intravenous loading dose of phenytoin or phenobarbital. Careful use of intravenous diazepam is sometimes useful in helping to achieve these objectives. Intravenous phenytoin and phenobarbital provide definitive, long-term control of tonic-clonic seizures but must be administered slowly and require time to reach peak brain concentrations. Intravenous diazepam appears to enter and exit from the brain rapidly and may control seizures while therapeutic brain concentrations of long-acting drugs are being achieved. Phenytoin, phenobarbital, and diazepam should not be administered intramuscularly in treating status epilepticus. Treatment of focal motor and complex partial seizure status epilepticus is similar to that of tonic-clonic status epilepticus, except that intravenous diazepam is less frequently required and loading doses of phenytoin and phenobarbital can sometimes be given more slowly. Status epilepticus of the absence type is managed with intravenous acetazolamide or diazepam. Paraldehyde, muscle relaxants, general anesthesia, and lidocaine may be tried when conventional therapies fail.

Status epilepticus is defined as seizures occurring so frequently that the patient does not fully recover from one seizure before having another. The different types include tonic-clonic (grand mal), focal motor, complex partial (psychomotor, temporal lobe), and absence (petit mal) status epilepticus. Tonic-clonic is the most common and most life-threatening form of status epilepticus.

TONIC-CLONIC (GRAND MAL) STATUS EPILEPTICUS

Definitions

Tonic-clonic seizures begin with loss of consciousness and generalized stiffening of the trunk and extremities, usually in extension (tonic phase). This is followed by symmetrical jerking and relaxation of the extremities (clonic phase). A patient is defined as having tonic-clonic status epilepticus if he is having repeated tonic-clonic seizures without fully recovering from the post-ictal phase (decreased responsiveness, confusion, disorientation) of one seizure before having another. Some authors also would classify ongoing tonic-clonic seizure activity lasting longer than 30 minutes as status epilepticus, even if the patient is having his first seizure. The clonic phase often decreases in duration in a patient with continuing tonic-clonic seizures.[1] The seizures are bilaterally synchronous at onset in 45% of cases.[1] In the remainder, seizures are adversive (head and/or eyes deviated to one side) or focal in onset.

Frequency and Significance

The reported frequency of tonic-clonic status epilepticus among patients with epilepsy varies from 1 to 5%.[2-5] The mortality of tonic-clonic status epilepticus at the turn of the century was 10 to 50%.[6] The reported mortality currently is 6 to 18%.[3,4,7,8] Death during tonic-clonic status epilepticus may be due to circulatory collapse, to overmedication, or to the basic disease process causing status epilepticus. Tonic-clonic status epilepticus causes one-third of all epilepsy-related deaths.[2] Animal studies indicate that prolonged seizure activity, even in paralyzed, respirated animals, may result in irreversible cerebral damage.[9-11]

Management of Patients with Tonic-Clonic Status Epilepticus

Maintenance of Vital Functions. The patient should be positioned to avoid aspiration, suffocation, or falls. A soft plastic oral airway should be taped in place if it is possible to do so without forcing the teeth apart. Forcing an airway between clenched teeth may result in dental injury and aspiration of teeth. Wooden tongue blades may cause injuries from splinters and cuts. Spoons and other objects made of metal may injure teeth. Intubation may be necessary to maintain respiration. A large intravenous catheter should be placed for administration of medication and fluids. It is always prudent to administer a bolus of intravenous dextrose (eg, 50 ml of a 50% solution) to any patient with altered consciousness as soon as blood for routine laboratory determinations is obtained. Thiamine (eg, 50 mg intravenously plus 50 mg intramuscularly) should be administered before administering glucose if chronic alcoholism and/or alcohol withdrawal are suspected.

Identification and Treatment of Precipitating

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Factors. Most cases of tonic-clonic status epilepticus occur in patients with known chronic seizure disorders, but occasionally status is the presenting symptom. Over two-thirds of cases with tonic-clonic status epilepticus occur in patients with "symptomatic" (ie, due to a known structural or metabolic lesion) epilepsy; the remainder have "idiopathic" epilepsy.[2-5,7] The "symptomatic" lesions most commonly associated with tonic-clonic status epilepticus are tumors, post-traumatic injuries, central nervous system (CNS) infections, prenatal or perinatal injuries, and cerebrovascular accidents.[2-5,7] Occasionally, tonic-clonic status epilepticus seems to be precipitated by the massive size of a cerebral lesion without any other precipitating factor.

The majority of cases of tonic-clonic status epilepticus do not occur randomly or as a result of a massive cerebral lesion. Rather, there is a specific precipitating factor which causes a patient with a known seizure disorder to develop status. The most frequent causes are withdrawal from antiepileptic drugs, and activation of a seizure disorder by fever.[2,3,7] Other precipitating factors include: (1) withdrawal from alcohol or sedative drugs, (2) metabolic disorders (hypocalcemia, hyponatremia, hypoglycemia, hepatic or renal failure), (3) sleep deprivation, (4) acute new central nervous system insult (meningitis, encephalitis, cerebrovascular accident or trauma), (5) diagnostic procedures (pneumoencephalogram, cerebral angiography, etc.), and (6) drug intoxication (eg, tricyclic antidepressants, isoniazid).[3,7,8,12,13] Precipitating factors must always be vigorously sought and treated to facilitate seizure control and to insure that any reversible cause of cerebral dysfunction is treated before it causes irreversible damage.

Treatment of Seizures. To control status epilepticus quickly and to prevent its recurrence, a therapeutic serum concentration of a long-acting antiepileptic drug must be quickly achieved and maintained. A long delay in achieving a therapeutic steady-state serum concentration of drug will occur if the drug is begun in its usual maintenance dosage.[14-16] The time required to reach steady-state serum concentration after beginning a fixed maintenance dosage is 7 to 8 days for phenytoin and 14 to 21 days for phenobarbital.[15,16] To obtain rapidly a therapeutic steady-state serum concentration when a drug is begun it is essential to give a proper loading dose of drug. Readers not thoroughly familiar with the concept of the loading dose should consult an article on basic pharmacokinetics.[14]

The question of how much drug to give to a patient who is already supposedly taking antiepileptic medication is a complicated one. If antiepileptic drug serum concentration determinations are immediately available from the clinical laboratory or from medical records, they can guide therapy. If a patient has a high therapeutic serum concentration of a drug, then a full loading dose of a different drug should be given. If the patient has a drug serum concentration in the low or middle part of the therapeutic range, then a loading dose of the drug sufficient to produce a high therapeutic serum concentration should be given. Assuming a one-compartment model with first order elimination kinetics, the loading dose necessary to produce a high therapeutic serum concentration is calculated as follows:

$$\text{loading dose} = 2 \times \left[\frac{\text{desired serum concentration}}{\text{observed serum concentration}} - 1\right] \times D \times t_{1/2}$$

where D is the daily dosage of drug and $t_{1/2}$ is the elimination half-life of drug in days. In practice this formula is only a first approximation of the proper loading dose because: (1) patients often do not take all of their prescribed medication, and the observed serum concentration is less than it should be; (2) the elimination half-life of a given drug varies among patients, and the "average" half-life of a drug may be quite different from that in a particular patient; and (3) some drugs, especially phenytoin, do not follow first-order elimination kinetics over the entire range of therapeutic serum concentrations. If the calculated loading dose is greater than the usual loading dose for patients on no medication (as will happen in noncompliant patients), the usual loading dose should be given.

Often one is confronted in the emergency room with a patient in tonic-clonic status epilepticus who supposedly takes one or more antiepileptic drugs for whom recent antiepileptic drug serum concentration data are not available. It is usually best to give such patients a full loading dose of the antiepileptic drug of choice (if vital signs and electrocardiogram remain stable during drug administration) rather than a partial loading dose because: (1) failure to take medication is one of the most common causes of status epilepticus; (2) true tonic-clonic status epilepticus is rare in patients with high therapeutic serum concentrations of phenytoin or phenobarbital; (3) the usual side effects of an excessively high serum concentration of phenytoin or phenobarbital (drowsiness, ataxia, dysarthria, diplopia) will reverse as the serum concentration falls; and (4) the risks of continued tonic-clonic status epilepticus are usually greater than risks of the usual side effects of high serum concentrations of antiepileptic drugs.

Drugs Used to Treat Tonic-Clonic Status Epilepticus

Phenytoin

Indications. Phenytoin is the antiepileptic drug of choice for most patients with tonic-clonic status epilepticus because: (1) phenytoin is extremely effective in controlling tonic-clonic status epilepticus,[17-19] (2) an intravenous loading dose of phenytoin can be rapidly and safely administered (see below), (3) phenytoin does not depress respiration as much as alternative drugs, (4) phenytoin does not depress the level of alertness as much as alternative drugs and thus better allows the evaluation of men-

Table 1

Serum Concentration of Phenytoin After Single Intravenous Loading Doses of Sodium Phenytoin in Adults

Dosage (mg/kg)	Infusion Rate (mg/min)	Serum Concentration (μg/ml) Peak Mean	Peak Range	1 Hour Mean	1 Hour Range	24 Hours Mean	24 Hours Range	Reference
2.0[a]	62.5	8.8		4.7				20
3.3[b]	50	10.5	3.9-17.4	5.2	3.8-6.4	1.9	1.0-2.4	21
3.6[c]	25	7						22
3.4-4.2[d]	50	12.7	9.9-18.2	7.9	6.9-9.1	2.6	1.6-3.8	23
5.0	50[g]		9-11					24
5.0	25	12						25
7[e]	100[g]	17	10-24	9	6-11			18
7.5	37.5	19						25
10.7	25		8-25					26
12	50[g]					7.1		27
10.9-17.2 (mean 13.0)	80[g]	31.5	17-59	16.3	8-27	7.9	3-19	19
14[f]	100[g]	19	12-32	17	12-30			18
18	50[g]			23.5		15.0		27

a: 5 adults with mean weight of 67 kg given 125 mg
b: 6 adult males with mean weight of 75 kg given 250 mg
c: 12 adult males with mean weight of 70.0 kg given 250 mg
d: 6 adult males given 300 mg
e: 5 volunteers given 500 mg intravenously and 500 mg intramuscularly
f: 33 patients given 1000 mg intravenously and 500 mg intramuscularly
g: maximum rate of infusion employed in study, rate less in some patients

tal status, (5) if adjunctive therapy with diazepam is required, diazepam probably causes less cardiorespiratory depression in combination with phenytoin than in combination with phenobarbital or paraldehyde, and (6) phenytoin is the antiepileptic drug which has the best therapeutic index for the chronic treatment of tonic-clonic seizures in most adult patients.

Contraindications and Warnings. Phenytoin is contraindicated in patients with a history of hypersensitivity to hydantoins. Because of its effect on ventricular automaticity, phenytoin should be given only with great caution to patients with sinus bradycardia, sino-atrial block, second and third degree A-V block, and Adams-Stokes syndrome. Phenytoin should also be used with caution in patients with hypotension and severe myocardial insufficiency. In certain situations (see below) it may be decided that phenobarbital would be a better chronic antiepileptic drug than phenytoin. These patients should be treated with a loading dose of phenobarbital rather than phenytoin.

Pharmacokinetics and Dosage. The therapeutic range of phenytoin serum concentration during chronic oral administration for prevention of tonic-clonic seizures is 10 to 20 μg/ml.[15,16] Wallis, et al[18] reported serum phenytoin concentrations of 13 to 32 μg/ml in patients whose status epilepticus was successfully treated with intravenous phenytoin. The pharmacologic objectives in using intravenous phenytoin to treat status epilepticus are to produce a therapeutic serum concentration (10 to 20 μg/ml) of phenytoin as rapidly as possible, and then to maintain this concentration without excessive fluctuations. Administration of the usual daily dosage of phenytoin (64 mg/kg) as a single intravenous injection does not always produce a therapeutic serum concentration, even initially; within 1 hour of the dose, serum levels can fall to the subtherapeutic range (Table 1). An initial dose of 7 mg/kg produces therapeutic levels initially, but again these can fall to the subtherapeutic range within one hour of administration. A loading dose of 13 mg/kg of phenytoin will produce high therapeutic serum concentrations for 6 hours.[19] A desirable dosage schedule[18] consists of administration of 14 mg/kg of phenytoin as an intravenous loading dose, followed by maintenance doses of 100 mg orally or intravenously every 6 to 8 hours. This approach consistently produces high therapeutic phenytoin serum concentrations throughout the 24-hour period after the loading dose.[18] If a similar loading dose is given and maintenance therapy not begun for 24 hours, the serum concentration of phenytoin will often fall to subtherapeutic levels within 6 to 24 hours.[19]

The above data are for adults. Recent work indicates that a loading dose of 15 to 20 mg/kg of phenytoin in neonates will produce a serum concentration of 12 to 18 μg/ml.[28] Orally-administered phenytoin is not well absorbed in neonates, and maintenance doses of the drug must be given intravenously to maintain a therapeutic serum concentration.[28]

If intravenous phenytoin is administered at the recommended maximum rate of 50 mg per minute, it will take approximately 20 minutes to administer a full loading dose to an adult. Peak brain and cerebrospinal fluid levels may not be reached until approximately one hour after completion of the infusion.[19] Thus, if a loading dose of phenytoin is infused as the only medication for status epilepticus, seizures may continue during the infusion and for as long as one hour after the infusion is completed.[19]

Diazepam is often a useful adjunctive drug to control tonic-clonic status epilepticus in the period while phenytoin serum and brain concentrations are rising (see below).

Intramuscularly administered phenytoin is very slowly absorbed.[18,22] Peak serum phenytoin concentrations occur approximately 24 hours after a single intramuscular injection and are significantly lower than those produced by the same dose given intravenously.[22] Intramuscular phenytoin should never be used in the treatment of status epilepticus or any other medical emergency where a therapeutic phenytoin serum concentration must be rapidly and predictably achieved.

Administration. Intravenous phenytoin should be given at a rate no greater than 50 mg per minute. The only method for administering intravenous phenytoin approved by the Food and Drug Administration is direct intravenous bolus. Mixing of the drug with intravenous fluids (especially those with glucose) may lead to precipitation. Heart rate, blood pressure, and the electrocardiogram should be monitored frequently during the administration of a loading dose. Phenytoin sodium for injection is an irritating substance that can cause chemical phlebitis and, if extravasated, tissue damage. Therefore the following precautions should be observed when administering intravenous phenytoin: (1) use a large infusion catheter in a large vein, (2) each injection of phenytoin should be followed by an injection of sterile saline (this is less likely to precipitate phenytoin than a glucose solution), and (3) extravasation should be avoided.

Toxicity. Reported serious complications of intravenous phenytoin include hypotension, atrial and ventricular conduction disturbances, ventricular fibrillation, cardiovascular collapse, and respiratory arrest. Serious complications are most likely to occur with rapid infusion, in the elderly, and in the gravely ill.[29] Less serious complications include drowsiness, circumoral tingling, vertigo, nausea, and, rarely, vomiting. These side effects usually occur when the serum phenytoin concentration is greater than 20 μg/ml.

The actual incidence of serious complications with full loading doses of intravenous phenytoin is quite low. Cranford, et al[27] administered loading doses of 10.5 to 25.3 mg/kg of phenytoin with electrocardiogram and blood pressure monitoring on 159 occasions for the control of seizures. There were only two serious complications (both reversible) — respiratory arrest and hypotension requiring termination of the phenytoin infusion. However, the investigators did report that 25% of patients had a fall in diastolic blood pressure of more than 10 mmHg and that this fall usually normalized with a decreased infusion rate.

Phenobarbital

Indications. Phenobarbital is indicated for the treatment of tonic-clonic status epilepticus in the following groups of patients: (1) those allergic to phenytoin, (2) those with evidence of disorders of cardiac conduction or automaticity, (3) those who continue to seize despite a full loading dose of phenytoin, and (4) those in whom it may be decided before treating that phenobarbital would be a better chronic antiepileptic drug than phenytoin. Examples of the last category include: (1) persons who have taken phenytoin in the past and discontinued the drug because of unacceptable side effects (eg, gingival hyperplasia and hirsuitism in a young woman), (2) in neonates, because they absorb oral maintenance doses of phenobarbital but do not absorb oral maintenance doses of phenytoin,[28] and (3) in children under 6 years of age because phenytoin may stimulate rather than inhibit seizure activity in the immature brain[30] and because of the possible effects of phenytoin or developing connective tissue.[31]

Contraindications, Warnings, and Administration. Phenobarbital is contraindicated in patients with hypersensitivity to any barbiturate or with porphyria. Intravenous phenobarbital usually causes sedation and may cause hypotension or respiratory depression. The drug should be used with care in patients with impaired respiratory, cardiac, hepatic or renal function and in patients with myasthenia gravis and myxedema. The cardiorespiratory depressant effects of phenobarbital and diazepam may be additive[32] and special caution must be used when these two drugs are given in combination. Solutions for intravenous injection should be freshly prepared and administered no faster than 60 mg per minute.

Pharmacokinetics and Dosage. The therapeutic range of phenobarbital serum concentrations in the management of epilepsy is 15 to 40 μg/ml.[15,16] Although penobarbital has been used as an antiepileptic drug since 1912, there has never been a systematic study of the dosage of intravenous phenobarbital necessary to achieve this range of serum concentrations. In a single study of neonates, intravenous loading doses of 15 to 20 mg/kg produced a mean ($\pm$SD) peak serum concentration of 19.4 $\pm$ 3.4 μg/ml.[28] If this loading dose was followed by a maintenance dose of 5 mg/kg/day by any route, therapeutic serum concentrations were maintained.[28] The ratio of peak serum concentration (μg/ml) to dose (mg/kg) of phenobarbital following a single oral or intramuscular dose is approximately 1.5:1.[33,34] It would appear that the proper intravenous loading dose of phenobarbital is between 8 and 20 mg/kg, followed by a maintenance dosage of 5 mg/kg/day in the first few days after status epilepticus. After that, the dosage should be adjusted to maintain a therapeutic serum concentration.

Peak serum levels occur 1 to 12 hours after intramuscular injections of phenobarbital.[33,35] The bioavailability of intramuscular phenobarbital has never been determined. The drug should not be given by intramuscular injection in the treatment of status epilepticus because: (1) peak phenobarbital

TABLE 2*

SUMMARY OF REPORTED EFFECTIVENESS OF DIAZEPAM IN VARIOUS TYPES OF STATUS EPILEPTICUS

Type of Status Epilepticus	Number of Reports	Number of Patients	Effect on Status Epilepticus: No Effect	Temporary Control	Lasting Control
Tonic-Clonic (Grand Mal)	19	188	23 (12%)	37 (20%)	128 (68%)
Secondarily Generalized Tonic-Clonic	6	38	4 (10%)	6 (16%)	28 (74%)
Focal Motor (Including Unilateral and Jacksonian)	17	103	13 (13%)	15 (15%)	75 (73%)
Absence (Petit Mal)	10	30	2 (7%)	3 (10%)	25 (83%)
Myoclonic	9	28	4 (14%)	4 (14%)	20 (71%)
Complex Partial (Psychomotor, Temporal Lobe)	4	8	2 (25%)	1 (13%)	5 (62%)
Tonic	4	8	3 (38%)	0	5 (62%)
Clonic	3	9	1 (11%)	0	8 (89%)
Hemiclonic	2	22	2 (9%)	6 (27%)	14 (63%)
Infantile Myoclonic	2	5	0	4 (80%)	1 (20%)

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serum concentrations are not reached rapidly, (2) the patient will continue to seize until the serum level has risen into the therapeutic range, and (3) toxic quantities may eventually accumulate if the patient is given multiple intramuscular injections.

Diazepam

Indications. Intravenous diazepam has a relatively brief duration of action and is not a definitive therapy for status epilepticus. However, given at the onset of therapy it can temporarily control seizures while precipitating factors are being treated and a loading dose of a long acting drug is being administered. Intravenous diazepam is indicated in the early management of tonic-clonic status epilepticus when: (1) generalized tonic-clonic activity has proceeded without interruption for more than a few minutes; (2) a tonic-clonic seizure occurs in a post-ictal patient who is being evaluated and is receiving a loading dose of a long-acting antiepileptic drug. (Since status epilepticus may end spontaneously, intravenous diazepam should not be administered to a patient who arrives at the hospital in a post-ictal state unless he has another seizure.) In practice, many patients with tonic-clonic status epilepticus will meet one or both of these criteria. The effectiveness of diazepam in controlling tonic-clonic status epilepticus is documented in Table 2.

The use of intravenous diazepam to control refractory tonic-clonic status epilepticus after a full loading dose of phenytoin or phenobarbital has been administered and apparently failed requires considerable medical judgment. Most cases of status epilepticus caused by failure to take medication or fever quickly respond to a loading dose of phenytoin or phenobarbital plus antipyretic measures if necessary. Cases of refractory tonic-clonic status epilepticus are unusual, and usually due to large brain tumors or to large acute cerebral insults (eg, encephalitis). In these cases judicious use of the smallest effective dose of intravenous diazepam to temporarily control the seizures is indicated if the seizures compromise vital functions. Care must be exercised in using diazepam in this situation because of additive cardiorespiratory toxicity when diazepam is given to a patient with a high serum concentration of another depressant drug. The major objective of the management of refractory tonic-clonic status epilepticus should be to treat precipitating factors and to add appropriate additional long-acting antiepileptic drugs (see below). Management of refractory tonic-clonic status epilepticus with repeated doses of diazepam frequently results in accumulation of toxic concentrations of diazepam and/or active diazepam metabolites.

Contraindications and Warnings. Diazepam is contraindicated in patients with known hypersensitivity to the drug or glaucoma. Because of possible cardiorespiratory depression, extreme care must be taken in administering intravenous diazepam to the elderly, the very ill, patients with limited pulmonary reserve, patients in shock, and patients who have received sedative drugs (including alcohol).

Probably the most common, and most dangerous, error made in the management of status epilepticus is to treat repeated seizures with repeated doses of intravenous diazepam without definitively treating the precipitating factors and without administering an adequate loading dose of a long-acting antiepileptic drug. In this situation, the patient will continue to seize and toxic concentrations of diazepam and/or diazepam metabolites may accumulate, with resultant morbidity.

Another frequent error is to administer intravenous diazepam to patients who are not truly in tonic-clonic status epilepticus, such as (1) those who had several tonic-clonic seizures before coming to the hospital but who arrive fully alert, (2) patients arriving at the hospital fully alert, then having a single tonic-clonic seizure, and (3) those arriving in a post-ictal state after a single tonic-clonic seizure. Administration of intravenous diazepam to these patients exposes them to an unnecessary risk.

Pharmacokinetics. Electroencephalographic studies indicate that serum diazepam concen-

trations of at least 0.5 μg/ml are needed to control interictal paroxysmal activity.[36] Injection of 10 mg of diazepam intravenously in adults over 1 to 2 minutes produced peak serum concentrations of 0.3 to 2.0 (mean 0.9) μg/ml in one study.[36] Rapid injection of 20 mg intravenously in adults produced a mean serum concentration of 1.6 μg/ml in another study.[37] The disappearance of diazepam from serum follows a bi- or triphasic curve. Immediately after an intravenous injection of diazepam the "distribution phase" ($t_{1/2\alpha}$) half-life is 16 to 90 minutes.[36,38] The later "elimination phase" ($t_{1/2\beta}$) half-life is much slower.[36,38] Serum diazepam concentrations frequently decrease by more than 50% during the first 20 minutes after intravenous injection[36] due to rapid and extensive distribution. This probably accounts for the frequent recurrence of seizure activity when diazepam alone is used to control status epilepticus.[32]

Animal work indicates that maximal diazepam concentration in brain is reached one minute after the end of an intravenous infusion.[39] Brain concentrations then fall rapidly in parallel with serum diazepam.[39] Brain concentrations of phenytoin and phenobarbital rise more slowly after an intravenous injection of drug, but the brain levels tend to remain relatively constant despite falling serum concentrations.[19,39] This is consistent with the well-accepted therapeutic strategy of initial use of intravenous diazepam for immediate seizure control, followed by prompt administration of a loading dose of phenytoin or phenobarbital to maintain seizure control when serum and brain concentrations of diazepam fall below the therapeutic range.[19,39]

Intramuscular diazepam is relatively slowly absorbed. Peak serum concentrations are reached approximately 60 minutes after an intramuscular injection.[37,40,41] Furthermore, the peak levels following intramuscular injection are lower than those following intravenous injection. In the study of Hillestad, et al[37] the mean peak serum diazepam concentration was 1.6 μg/ml after a rapid 20 mg intravenous injection and 0.3 μg/ml after a 20 mg intramuscular injection. Thus, intramuscular diazepam should not be used to treat status epilepticus because the onset of action is too slow and because even large doses may not produce effective antiepileptic serum concentrations.

Dosage and Administration. The usual initial adult dosage of diazepam for tonic-clonic status epilepticus is 5 to 10 mg intravenously at a rate of no more than 5 mg per minute. In children 5 years or older, the recommended dose is 1 mg every 2 to 5 minutes up to a maximum of 10 mg. In infants over 30 days of age and children under 5 years of age, the recommended dosage is 0.2 to 0.5 mg slowly every 2 to 5 minutes up to a maximum of 5 mg. The efficacy and safety of parenteral diazepam has not been established in infants younger than 30 days of age.

Because parenteral diazepam is locally irritating, it should not be administered into small veins and care should be taken to avoid extravasation or intraarteral injection. Diazepam should not be mixed with intravenous fluids.

Toxicity. The most worrisome complications of intravenous diazepam are respiratory depression and hypotension. In an earlier review[32] we found 26 cases of respiratory depression and/or cardiac depression among 401 cases of various types of status epilepticus treated with diazepam. The incidence of cardiorespiratory depression is probably greater when diazepam is given in combination with other depressant drugs.[32] Animal work indicates that some of the adverse cardiorespiratory effects of intravenous diazepam (and intravenous phenytoin) may be due to the propylene glycol solvent used in preparing the parenteral product.[42] Other less serious side effects of intravenous diazepam include drowsiness, ataxia, dysarthria, confusion, paradoxical excitement, and diplopia.

Other Agents Used in "Refractory" Cases

Most cases of "refractory" tonic-clonic status epilepticus occur because precipitating factors are not treated or because the dosage of phenytoin and/or phenobarbital administered is not sufficient to reach or maintain a therapeutic serum concentration. However, a small number of cases do not respond to therapeutic serum concentrations of these drugs. Such patients usually have a large brain tumor or a large acute cerebral lesion (eg, encephalitis) and present a difficult therapeutic problem.

Patients who continue to seize despite a full loading dose of either phenytoin or phenobarbital should then receive a loading dose of the other agent. If this fails, the following alternatives can be tried.

Paraldehyde. The older neurologic literature indicates that paraldehyde may be an effective drug in controlling status epilepticus.[43-45] It is no longer commonly used because of the following problems: (1) intravenous paraldehyde can cause pulmonary edema, pulmonary hemorrhage, and circulatory or respiratory collapse, (2) intramuscular paraldehyde is very painful and can cause tissue necrosis and damage to nerves near the injection site (eg, sciatic), (3) oral or rectal paraldehyde can cause corrosion of local mucosa, and (4) paraldehyde by any route has a disagreeable odor and taste and may cause a rash or toxic hepatitis. Despite these objections, a trial of paraldehyde may be indicated in a patient with tonic-clonic status epilepticus not controlled by phenytoin and phenobarbital.

The dosage of paraldehyde for status epilepticus is 0.1 to 0.15 ml/kg by the intravenous or intramuscular route. This dosage may be repeated every 2 to 4 hours if necessary. Peak blood levels are reached 20 to 60 minutes after intramuscular injection and the elimination half-life of paraldehyde is between 3 and 10 hours.[46] Intravenous paraldehyde should be used only in emergency situations. It should be diluted ten-fold with normal saline and injected

slowly. Because paraldehyde is incompatible with many plastics, plastic equipment should not be used for storage or administration of the drug. Intramuscular paraldehyde should be injected undiluted deep into the buttocks, taking care to avoid the sciatic nerve and administering a maximum of 5 ml per injection site.

Muscle Relaxants (Curarization). Curarization will prevent tonic and clonic movements and physical injury and will allow control of respirations.[17] However, this form of treatment does not prevent ongoing cerebral seizure activity. Animal studies indicate that prolonged seizure activity, even in paralyzed, respirated animals, may result in irreversible cerebral damage.[9-11]

General Anesthesia. General anesthesia prevents tonic and clonic movements and allows for control of respirations. General anesthesia also has the advantage of reducing cerebral seizure activity and reducing cerebral metabolic needs. The general anesthetic agent of choice and the proper duration of anesthesia for treating status epilepticus are unknown. A nonflammable anesthetic should be used if the electroencephalogram is used to monitor the effect of anesthesia upon cerebral paroxysmal activity.

Lidocaine. Intravenous lidocaine may be effective in controlling tonic-clonic and focal motor seizures.[48-50] Bernhard and Bohm reported that 49 of 63 attacks of tonic-clonic and "Jacksonian" status epilepticus were "cut short" with intravenous lidocaine.[50] These authors recommend initiating intravenous lidocaine therapy with a single dose of 2 to 3 mg/kg. If the seizures do not stop, they may be refractory to lidocaine. If the seizures stop and then recur, they recommend beginning a lidocaine infusion at a rate of 3 to 10 mg/kg/hour.

Before administering intravenous lidocaine for seizures one should be aware of the following precautions: (1) epilepsy has not been approved by the Food and Drug Administration as an indication for lidocaine, (2) in high doses lidocaine may cause convulsions, (3) constant electrocardiogram and blood pressure monitoring is necessary to detect possible cardiovascular complications, (4) lidocaine should not be injected faster than 25 to 50 mg per minute, (5) the dosage recommended by Bernhard and Bohm[50] may exceed the maximum recommended dosage in the package insert (200 to 300 mg per hour), and (6) evidence for proper usage in children is limited.

Other Forms of Status Epilepticus

Focal Motor

Focal motor status epilepticus may take the form of focal or unilateral tonic and/or clonic movements.[1] Potential risks and benefits of treatment should be weighed before treatment is initiated. Intravenous diazepam usually will temporarily halt focal motor status epilepticus (see Table 2), and an intravenous loading dose of phenytoin often will completely end the attack.[18,19] However, there is some risk to administering intravenous diazepam and/or phenytoin (see above). If the focal motor seizures can be temporarily tolerated, it is less dangerous to administer an oral loading dose of phenytoin or phenobarbital. If 1000 mg of oral phenytoin is given over an 8 hour period, therapeutic phenytoin serum concentration will be reached in 6 to 12 hours after the loading dose and maximum concentrations reached in 30 to 40 hours.[51] An oral loading dose of phenobarbital consists of twice the maintenance dose for four days; this is followed by maintenance therapy. With this regimen steady-state phenobarbital serum concentration is reached in three days.[52] In patients whose focal motor seizures are not controlled with diazepam, phenytoin, and phenobarbital, a trial of oral carbamazepine or intravenous lidocaine (see above) may be helpful.

Complex Partial (Psychomotor, Temporal Lobe) Status Epilepticus

This rare form of status epilepticus may take the form of a prolonged period of confusion and automatic behavior or a series of partial seizures with postictal confusion in between.[8,53,54] Therapy of complex partial status epilepticus consists of an intravenous loading dose of phenytoin[19] or phenobarbital. Intravenous diazepam may terminate an attack (see Table 2) but carries some risk and is indicated only when the ongoing seizure activity threatens the patient's health and/or makes it impossible to administer a loading dose of a long-acting antiepileptic drug.

Absence (Petit Mal) Status Epilepticus

Absence status epilepticus consists of altered consciousness often accompanied by mild clonic movements of the eyelids and hands and automatisms of the face and hands.[1,55-57] The alteration of consciousness may range from a vague feeling which can only be recognized subjectively to stupor from which the patient can only be aroused with difficulty.[1,55-57] Attacks may last 30 minutes to 12 or more hours.[1,57] Although absence seizures occur mainly in children, a significant percentage of cases of absence status epilepticus occurs in adults.[1,57,58] Adults who have failed to "outgrow" absence seizures seem particularly prone to develop absence status epilepticus, and some adults with previously undiagnosed absence seizures may develop absence status epilepticus without a history of a seizure disorder.[57] The diagnosis is definitively established with an electroencephalogram.[1,55,57]

Therapy is complicated by the fact that ethosuximide, valproic acid, and clonazepam (the long-acting antiepileptic drugs of choice for absence seizures) are not available in a parenteral preparation and require several days to reach steady-state serum concentration when administered orally.[15,16,59,60] Acetazolamide is moderately effective but is seldom used because the effect is often tran-

sient and other drugs are more consistently effective.[61] In absence status epilepticus intravenous acetazolamide is usually the first drug to try because it causes fewer side effects than intravenous diazepam and because oral maintenance doses can be simultaneously begun. The dosage of intravenous acetazolamide is 250 mg for children less then 35 kg, and 500 mg for persons over 35 kg.

If acetazolamide fails to control absence status epilepticus, intravenous diazepam is usually very effective (see Table 2) although the effect may be transient. The patient may be managed with one or more doses of intravenous diazepam until an effective serum concentration of ethosuximide can be established by the oral route. Higher than usual starting doses of ethosuximide may be necessary to achieve a therapeutic serum concentration rapidly. An initial dose of 750 mg per day in divided doses produces relatively few side effects.[59]

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COUNTY SOCIETY NOTES — *Continued from Page III*

Announcement of the upcoming meeting of the International College of Surgeons in Fort Fairfield was made by Dr. Rideout.

It was moved, seconded, and voted that the Society recommend to the House of Delegates of the M.M.A. that Dr. Chester F. Hogan of Houlton be given Affiliate membership for 1977. Dr. Hogan is eligible for Senior membership in 1978.

Names were suggested for nomination from this Society to the M.M.A. Committee on Health Care Financing and to the Executive Council from this district. Suggestions were to be presented to the nominating committee.

The applications of Dr. Charles St. Pierre of Fort Kent and Dr. Laurence Watterson of Presque Isle were presented and they were elected to membership in the Society. The application of Dr. M. L. Carol St. Pierre of Washburn was likewise approved.

The position of the Society concerning health screening services was discussed but no formal action was taken.

GEORGE J. HARRISON, M.D., *Secretary*

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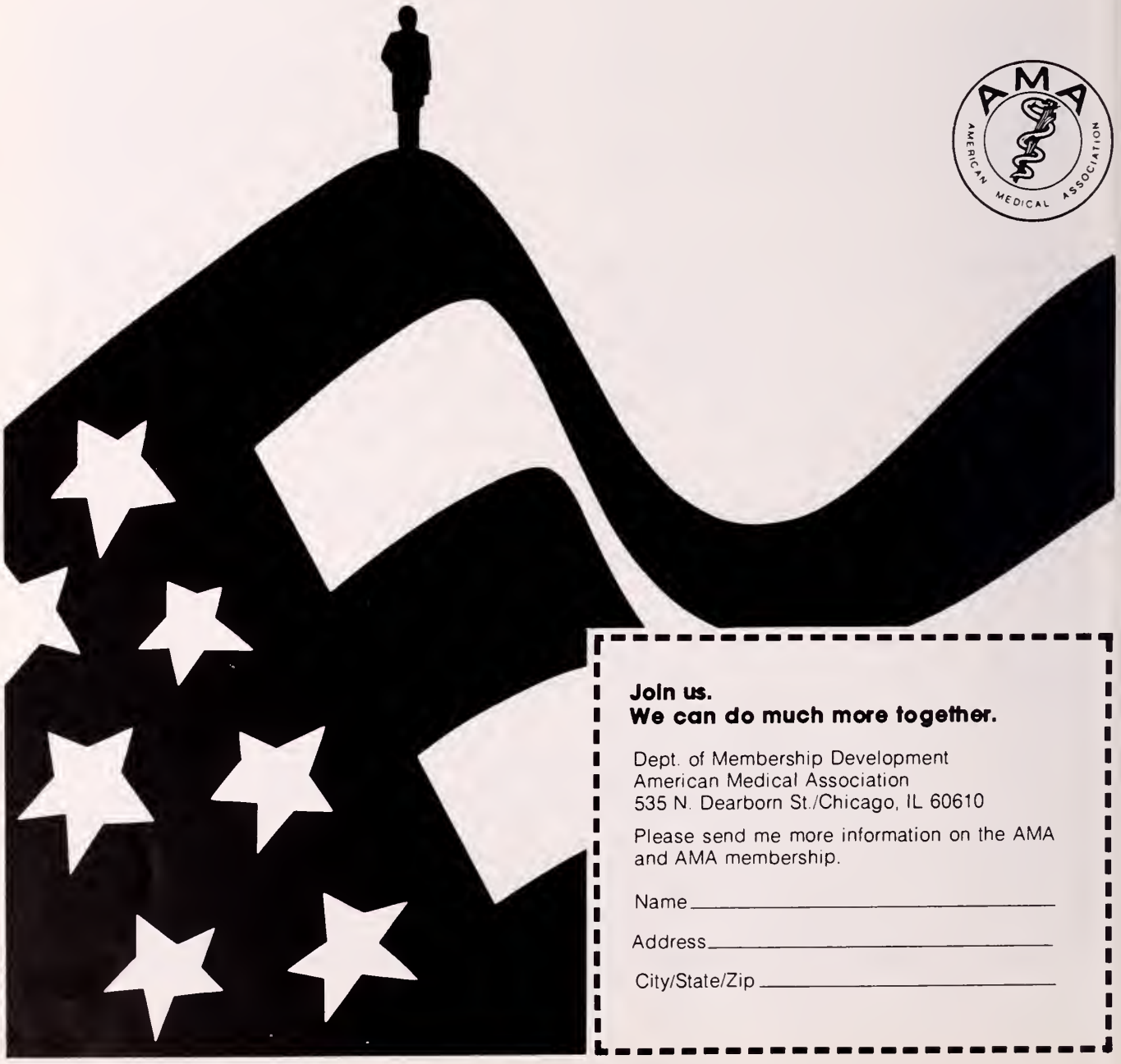

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The Journal
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Nodular Gastric Metaplasia

Confusion With Gastric Xanthelasma: Curiosity or Marker of Future Malignancy?

A Comprehensive Review of the Literature

GEORGE E. DAVIS, M.D.*

It is generally agreed that the human gastric ulcer (GU) has a more complex pathogenesis than that of duodenal ulcer (DU); at least the latter seems more clearly related to high HCL output. The gastric mucosal changes that permit GU without DU seem at least on the surface to be more complex. Certain prodromal or predisposing features tend to be consistent, i.e., chronic superficial gastritis tending toward atrophic gastritis and coupled with bile reflux along with *some* HCL set the stage for GU. The association of intestinal metaplasia (IM) in varying degrees, and dysplasia (each to be defined later) not only have an association with benign GU but also with malignant GU. Arguments in the literature concerning the significance of either IM or dysplasia as predictors of malignancy abound. Herein is described an unusually prominent gastric mucosal lesion which can serve as an axis for the discussion.

CASE REPORT

Patient J.B., a 53-year-old Caucasian woman, was first seen in 1975 for a chief complaint of "bloating." She had had a hiatus hernia repair the year before and in addition to the above complained of dysphagia, a problem she had had, even before surgery, for several years. Also, an UGI revealed a 1 cm. GU on the lesser curvature, a lesion which was assumed to be causing the "bloating" and fullness. She was admitted in May 1975 to St. Mary's Hospital, Lewiston for gastroscopy and biopsy. Except for an allergy to penicillin and a history of being S/P cholecystectomy, appendectomy, and panhysterectomy and physical examination was non-contributory. There was no use of ulcerogenic drugs and only moderate coffee intake and mild social ethanol consumption were noted. There had been no weight loss.

Upon attempted gastroscopy, it was found that an esophageal stricture 2 cm. below the cricopharyngeus would not permit passage of the instrument. Bougienage followed first with string-olives, then with Hurst bougies up to a 40 French (beginning with #23 Fr.). The Olympus GIF-D endoscope could then be passed without difficulty. Gastroscopy revealed a small, punched-out GU high on the lesser curvature surrounded by friable, inflamed mucosa. In addition, unusual pale yellow, elevated, circular islands of mucosa were noted on the lesser curvature, midbody, and antrum (Figs. 1 and 2). Biopsy results are reported below. Gastric pH in the unstimulated state varied from 7.0 to 7.5 and juice was bile-stained. After Histalog, however, pH fell to 2.8 — low but not achlorhydric.

The ulcer biopsy revealed granulation and fibrous tissue, infiltrated by lymphocytes and monocytes without evidence of malignancy. Biopsy of the yellowish nodules revealed intestinal metaplasia (IM) (see Fig. 3), epithelium thrown into papillary projections with the lamina diffusely infiltrated by plasma cells and a few neutrophiles.

Medical therapy for the GU was successful in healing the lesion to 3 mm. as of 6/12/75, and by 7/18/75 repeat gastroscopy proved complete healing but as expected the IM was unchanged. Because of persistent epigastric pain, a repeat UGI series was performed on 11/13/75 and again showed a 1 cm. benign-appearing GU on the lesser curvature, posterior aspect. Definite surgery was then recommended and performed on 12/3/75. Gastric ulcer (benign) was confirmed — the mucosa seemed atrophic, and submucous pale areas averaging 3 mm. diameter located extensively throughout the stomach were noted.

Microscopic examination as reviewed by Dr. M. Montes (see reference) revealed gastric wall showing changes of chronic hypertrophic gastritis with severe intestinal metaplasia, a distinct reduction in the number of oxyphilic cells, Paneth cells in the crypts of scattered metaplastic glands, hyperplasia of the gastric goblet cells, accentuation of the normal granular appearance of the mucosa (etat mammeloneé), and lymphoid nodule and lymphoid follicle formation. Scattered cystic dilated glands were observed. An Alcian blue stain gave a positive reaction for the goblet cells of intestinal metaplastic glands, but a negative one for

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the mucous-secreting cells of the remaining gastric glands. The P.A.S. stain gave a strongly positive reaction in both types of goblet cells. In the areas of IM, a good number of argentaffin cells were detected in the crypts of the glands. The gastric mucosa free of IM displayed only a few argentaffin cells. There was no evidence of malignancy.

The surgery performed was a subtotal gastrectomy without vagotomy (see Fig. 6).

Because of the size of the resection, a Schillings test performed 3 months post-operatively was done and was extremely low in value mandating vitamin B12 injections every month. In spite of B complex and B12 intake, the patient's tongue and mouth seemed to "burn" and she developed perleche presumably due to *Candida*.

Repeat esophagogastroduodenoscopy was done on 12/9/76. The gastric pouch was grossly normal except for some atrophy of folds and no discrete nodules were obvious as before surgery. There were no marginal ulcers. A silk stitch protruded at the anastomosis. At this point, methylene blue dye was introduced into the stomach via the gastroscope. Staining of the mucosa revealed more or less discrete circular areas approximately 3 mm. or slightly larger in diameter on the gastric folds highlighted by the dye, especially at the borders. Biopsies again revealed IM and the lamina showed quite intense diffuse infiltration by plasma cells and a few neutrophiles (see Figs. 4 and 5).

When last seen, the patient still was not completely free of symptoms; namely, a peculiar bloating sensation persisted after meals — similar to other Billroth II patients but more troublesome. The problem of esophageal stricture had not recurred as of 12/76; however, the possibility of bile rather than acid as an irritant may well be a future problem. The need, if any, to repeat endoscopy and at what intervals prompted this review.

Discussion

The phenomenon of metaplasia, first described by Kupffer in 1883, may be defined as a transformation of epithelial cells into an altered physical form usually intestinal in type — simple columnar cells, which may or may not function as producers of enzymes or other active substances. In the stomach, metaplasia is characterized by the presence of goblet cells, the *sine qua non* of this lesion.[1] The mucus produced by the goblet cells of IM is chemically distinct from that of mucus of normal stomach epithelium.[2]

The origin of IM is unknown but for want of better evidence has been generally agreed to be derived from a common stem cell which has differentiated to produce columnar, goblet cells, and Paneth cells.

The normal surface columnar epithelium of the gastric mucosa is secretory in function whereas the epithelium of IM is both absorptive and secretory. In IM, the gastric mucosa transforms to a small bowel absorptive type with a tendency to villus formation with a typical brush border (microvilli). The crypts are lined by columnar epithelium and Paneth cells are found at their bases. In fetal and normal gastric mucosa, Paneth cells are not found. It would seem justifiable to accept the presence of Paneth and goblet cells as pathognomonic of IM in gastric mucosa. Brush border enzymes and at least passive lipid transport have been demonstrated in such mucosa.[3]

The usual distribution of gastric IM is patchy; because it may be overlooked by many endoscopists its true incidence is unknown.[4] Nevertheless, many observers feel that the lesion is more common in patients with bile reflux and with varying degrees of atrophic gastritis.[5] Particularly common is its presence in the gastric pouch after ulcer surgery.

As previously stated, the true incidence of IM is not fully known. How assiduously an observer pursues the search often is proportional to the reported percentages. For example, Morson found that IM was present in 65.4% of stomachs resected for duodenal ulcer;[6] however, it must be noted that these were microscopic findings and not the relatively large lesions as shown in Fig. 2. Lesions as seen in the presented case are unusual even in patients with underlying GU where IM tends to be more common grossly as well as microscopically. It is clear too that the more biopsies taken (or sections in surgical specimens) the more likely to find the lesion of IM.[7] Most authors agree that IM is more commonly seen in older patients, thus it may represent part of the aging process itself.

The question of whether IM is related to gastric cancer remains unanswered as well. Of course, this is the most important question to be resolved because of the proven lethality of gastric cancer. However, there may also be "benign" symptoms associated with IM. This latter question has not even been addressed in the literature. Various authors have reported between 60- 100% of patients with gastric cancer have IM, the 100% for multicentric cancer. Morson, et al presented evidence of 33% of 107 primary gastric carcinomas arose from IM. Ironically normal small bowel epithelium transforms to malignancy extremely rarely. Why gastric IM should transform with any higher frequency is peculiar but certainly not without precedent in other ectopic tissues of the body (i.e., Barrett's epithelium of the esophagus). The Japanese literature is most complete in convincing us that IM transforms to cancer;[8] however, it is also known that gastric cancer seems to be a different disease in Japan as compared to other geographical areas. In Japan, 50% of all deaths by cancer in males and 30% in females are due to gastric carcinoma.[9] In expatriated Japanese, the relationship between IM and carcinoma is not nearly so intimately associated. An environmental factor (probably foodstuff) may well expain the very close association in Japan although that too is unknown.

Several papers have attempted to classify gastric carcinoma into two types — intestinal and diffuse, the former well-differentiated and rich in mucin and enzyme production and seen in the older age groups, and with an accompanying high incidence of IM; the latter, diffusely, infiltrating, signet-ring type seen more often in younger age groups. Unfortunately, gastric carcinoma is not always uniform in form or physiology even in the same patient and many authorities argue that the distribution of the histological types of gastric carcinoma is the same in spite of the difference in the incidence of IM. Korn has felt

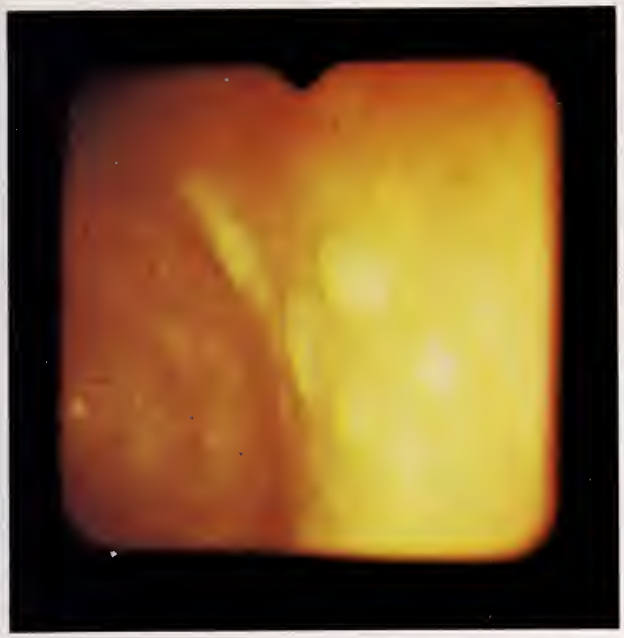

Fig. 1. Slightly elevated, pale nodules greater curvature antrum.

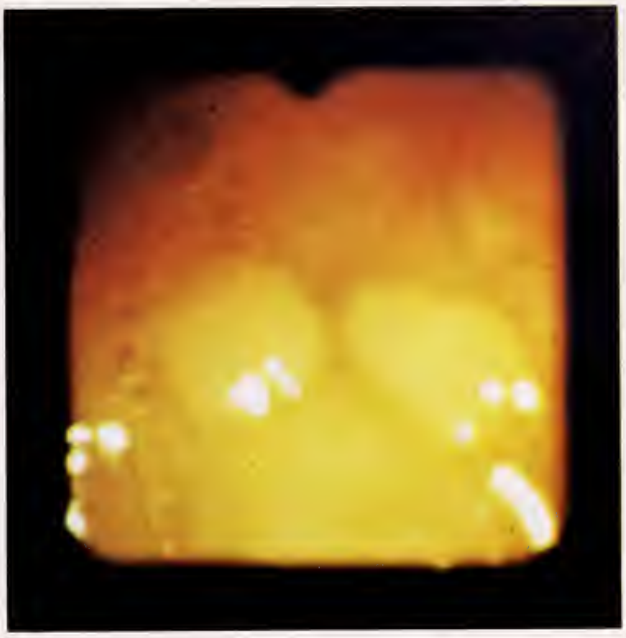

Fig. 2. Close-up of nodules.

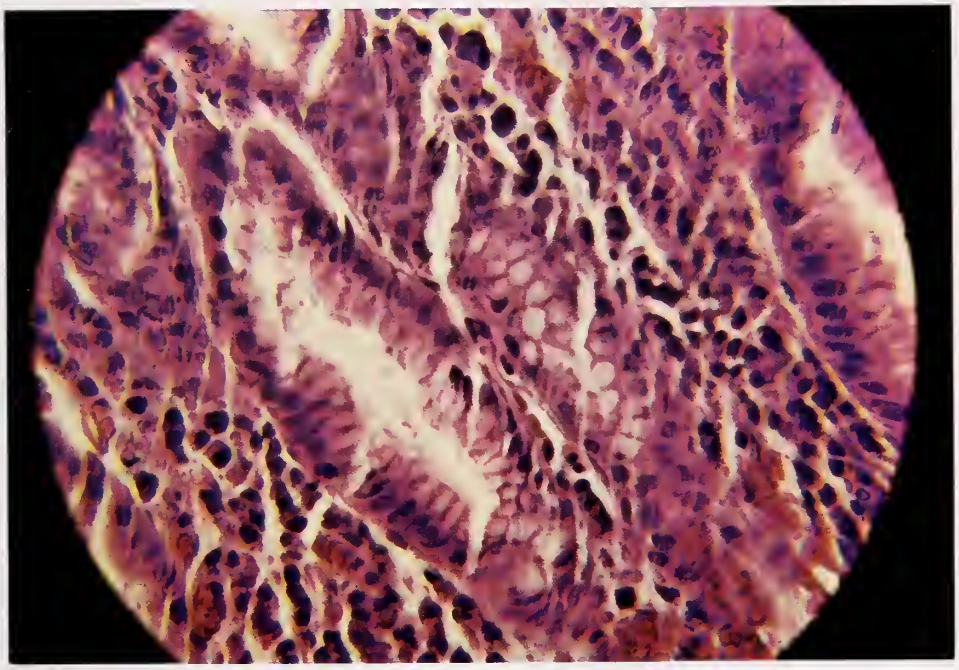

Fig. 3. Microscopic section of nodule.

that IM may lead to carcinoma and recommends frequent gastroscopic exams in following his patients with IM.[10] Domelloff found no convincing association between IM and carcinoma in his recent review of 459 patients.[3] Of these only three cases of stump carcinoma were found in those 140 patients (included in the 459 above) who were already deceased at the followup point — all at 17, 17, and 19 years post-op respectively. The total incidence in that study was 2% (carcinoma) when the still-living patients were included in the statistics. Those who were male amounted to 3.6%, thus the previously reported male predilection for stump carcinoma. Domelloff, because of the above late incidence, recommends repeated gastroscopic exams about 10 to 15 years after gastric surgery.

Schrumpf recently reported on 421 patients who had had gastrectomy 20 to 25 years prior and out of the 108 of these which were gastroscoped only 4 had infiltrating carcinoma and 3 had severe dysplasia, considered by that group to be a premalignant lesion. Surprisingly however, only 12% of the biopsy

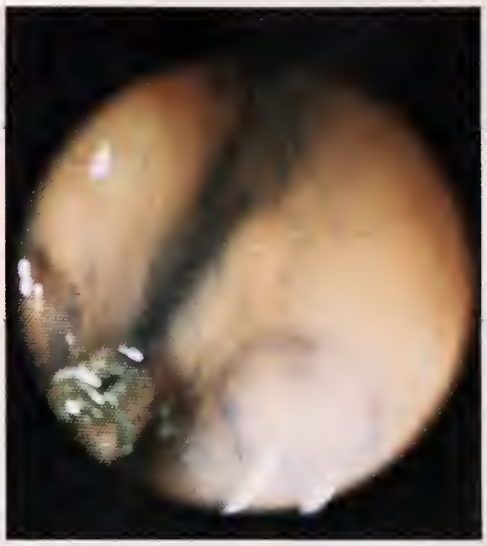

Fig. 4. (3 photos above). Easy demonstration of metaplastic areas using methylene blue dye. Note biopsy forceps in center photo (approximately 3 mm. diameter for reference). For reasons that are not clear, the margins of the lesion take up the dye more readily.

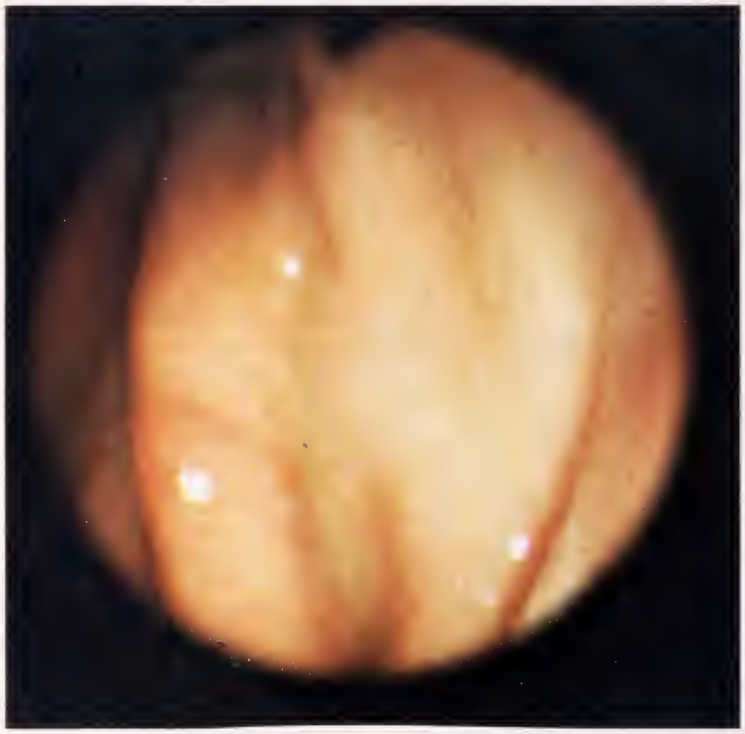

Fig. 5. Same mucosa without methylene blue.

specimens in those patients with carcinoma demonstrate the tumor.[11] No staining techniques were used — just a blind biopsy 2 cm. from the anastomosis (10 bites from the lesser curvature and 10 from the greater). Only one patient out of the 108 scoped had "normal" biopsies, 12/108 (11%) "gastritis", 24/108 (22%) IM, and 64/108 (59%) slight to moderate dysplasia. Schrumpf also recommended routine endoscopy of all patients 20 years or more after gastrectomy even though his study missed 2 cases (50%) of subsequently-proven carcinoma.

What really determines a logical outcome in these studies is accurate and uniform definition (and interpretation) of terms like "gastritis, metaplasia," and especially "dysplasia." IM has already been defined previously but dysplasia is really a matter of interpretation of the pathology — the difference between regenerative hyperplastic epithelium and dysplasia can be challenging. In both there is abnormality in size and shape of regenerating glands with diminished mucin production, and increase nuclear hyperchromasia, variation in nuclear size, and an increased mitotic rate. Severe changes like these in the absence of *inflammatory* cells are almost certainly compatible with dysplasia; however, in practice some degree of inflammation usually complicates the issue and accounts for the observed variation even by highly-trained individuals.

Suzuki described a proteolytic enzyme — methylene blue stain technique employed through the gastroscope to detect mucosal aberrancy.[12] Proteinase (Pronase) removed excess mucus and the dye absorbed to IM or dysplasia. The mechanism of this attraction has not been clarified. The patient presented here (see Case above) has islands of tissue later shown to be IM which were well outlined by a similar method using methylene blue dye alone.

When several experienced endoscopists were presented Fig. 2, the initial impression was "gastric xanthelasma" by at least two individuals. As it turned out the *sine qua non* of gastric xanthelasma (GX), namely foam cells in the lamina proptia, was not present; however in the functioning stomach the lesion in Fig. 2 did have a yellowish hue and suggested the presence of fat.[13] Although no detailed analysis of the lipid content was done in this case, lesions of IM in other cases have been so studied and found to contain cholesterol esters. Whether this is due to pinocytosis directly, diffu-

Fig. 6. Surgical specimen — Stomach everted shortly after excision. Antrum superior in photo. Ignore reflected light spots. Black arrows indicate nodules of intestinal metaplasia noted by gastroscopy.

sion, or lack of lymphatic exodus is not known but perhaps may be influenced by dietary factors, bile reflux, or even metabolic abnormalities like diabetes. In Kimura's review, in 1969, GX was found in 58% of 193 autopsies, single and multiple and not favoring any specific area of gastric lining.[14] The lesions were usually 1 — 2 mm. in diameter and like IM are more frequent with increasing age. No one has directly implicated GX with subsequent development of malignancy except in its association with IM.

Conclusions

Gastric intestinal metaplasia may be particularly impressive presenting as discrete nodules in the gastric mucosa which may grossly resemble gastric xanthelasma. It is generally agreed that IM (and GX) is more common in stomachs susceptible to GU and in the late post-operative stomach, possibly reflecting an accelerated aging process or uncertain mechanism but likely to implicate bile reflux in some fashion. Most workers also agree that there is a real increase in the likelihood of stump carcinoma in the range of 10 to 20+ years post surgery but that IM itself does not conclusively precede its development. Males seem to be more susceptible to the late-onset carcinoma. We must better define "dysplasia" especially in the presence of low-grade inflammatory cell infiltration. Even multiple biopsies may miss stump carcinoma but in spite of this most authors recommend repeated gastroscopic examinations 10 to 20+ years after surgery.

Acknowledgements

Special thanks to Dr. Mario Montes, Chief of Pathology at Buffalo Veterans Administration Hospital (1975), for his special stains of the material and to Dr. Joseph Houle, Dept. of Pathology, Augusta General Hospital, for his critical review. Also, to Dr. Gerard Morin for obtaining the surgical specimen and interest in the case and finally to Marthalie Prince for preparation of the manuscript.

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Continued on Page 214

Promiscuous ResusAnnies — A Public Health Problem?

A Plastic Typhoid Mary

GEORGE E. DAVIS, M.D.

Lately there has been an almost fanatical interest by paramedical and nursing personnel in CPR (Cardio-pulmonary resuscitation) and hospital staffs have encouraged and now have often mandated certification programs involving CPR. This is obviously beneficial to the general public. Even schoolchildren are being taught the pertinent anatomy of the ubiquitous ResusAnnie.

One possible harmful public health problem was brought to mind recently when I observed that almost invariably the mannequin was "sterilized" between "rescuers" by simple 70% alcohol. While I doubt that the fastidious *Neisseria, Mycoplasma, Chlamydia, Mima*, or *Herellea* could survive such a solution, I am less sure about *Herpes simplex* virus, and not at all sure about hepatitis B virus or the still relatively unstudied hepatitis Non A, Non B virus. Oral transmission of these viruses has been documented and their relative resistance to alcohol and iodine is notorious. Adding to this is the fact that hospital personnel, especially nurses and physicians, and of the latter especially surgeons, carry HB_s-Ag at a rate of 10 times that of the general population. Indeed high-risk personnel like IV teams and dialysis nurses may be 30 times more likely to disseminate the virus in various bodily secretions, including saliva. In practical terms, about one person out of a hundred hospital-based staff taking the CPR course will be potentially infectious. Statistically this may vary more or less, however. While an inoculum of infecting serum is known to be a trivial .0004 cc blood, the amount of *saliva* needed is not at all clear. If a "rescuer" has gingivitis, specks of blood mingling with the saliva may increase infectivity. This is indeed an age of contrasts when masks are often worn in rooms of patients with hepatitis and the ritual of gowns and gloves (expensive and unnecessary) serve only to isolate the patient from good nursing care, while promiscuous ResusAnnies roam the continent, unreported to their appropriate State Health Departments! I wonder if anyone would visit a dentist who only rinsed his instruments in 70% alcohol between patients?

An obvious solution to the problem would be to autoclave Annie between performances, a ritual which I doubt would permit more than one "rescue." A poor alternative, but workable, would be to use a solution of 2% glutaraldehyde — known to be toxic to viruses as well as bacteria (Cidex), followed by an ether-acetone mixture which has the property of dissolving certain viral structures (suggested for *H. simplex*). The effect of ether-acetone on the anatomy of ResusAnnie is still experimental and several hundred more FDA forms will have to be completed before this solution can be released to worldwide CPR Certification Programs.

ADDENDUM

Although no "epidemics" have been yet reported to the CDC, it is wise to keep an open mind on the subject — after all, we may not know what we're looking for!

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NODULAR GASTRIC METAPLASIA — *Continued from Page 213*

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Orthopedic Management of Pathologic Fractures in Metastatic Disease

PETER E. GIUSTRA, M.D., ROBERT S. FURMAN, M.D., JOHN W. WICKENDEN, M.D., ROGER W. WICKENDEN, M.D., and PAUL J. KILLORAN, M.D.*

As survival of patients with metastatic malignancy increases, so too does the incidence of pathological fractures from osseous metastases.

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The duration of patient survival often depends on medical, radiation and host responsiveness to the primary tumor. The quality of survival ultimately depends on proper management of the pathologic fracture.

Internal fixation in conjunction with Methylmethacrylate, the acrylic resin used in joint re-

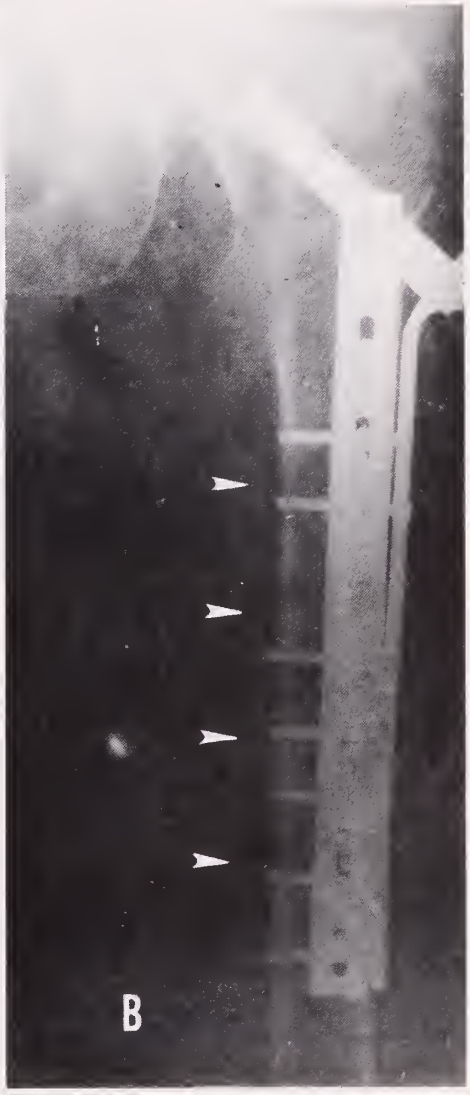


Fig. 1, A & B. Pathologic fracture of the left femur from carcinoma of the lung initially treated with a Smith Peterson nail, McLaughlin side plate and additional slotted plate. No Methylmethacrylate was used.

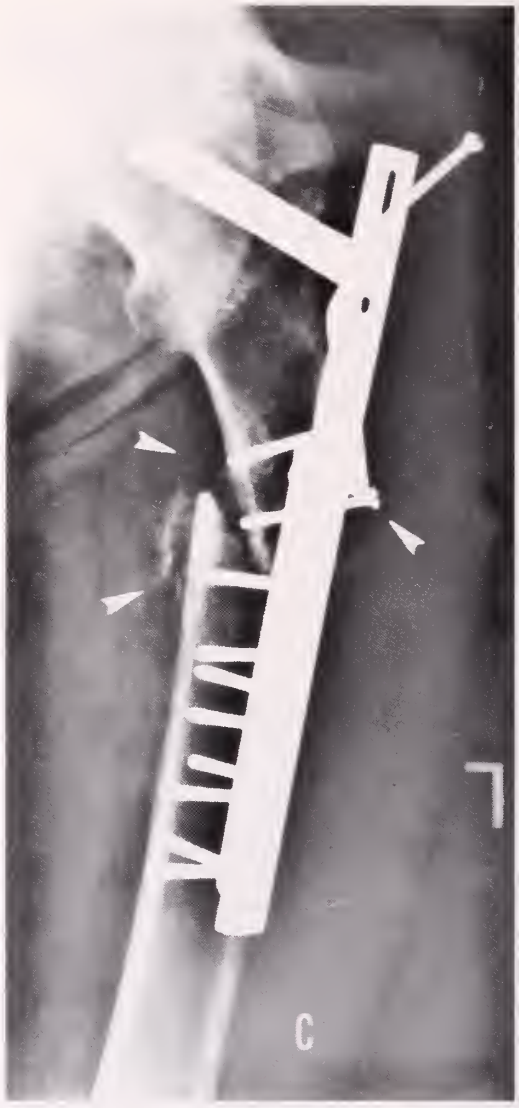


Fig. 1, C & D. Refracture of metastatic lesion and broken McLaughlin side plate 3 months later was treated successfully with a hip nail, Zickel rod, and Methylmethacrylate.

placement for benign disease, is now considered the primary treatment of choice for pathologic fractures in metastatic disease.[1-7] We wish to present our experience in 9 patients with histologically documented metastatic disease to bone so treated at the Penobscot Bay Medical Center.

Case Reports

Case 1. Broken McLaughlin side plate without Methylmethacrylate.

A 73-year-old female developed a pathologic fracture of the left femur following a one week history of left thigh pain. Subsequently, carcinoma of the lung was found. Initial treatment consisted of open reduction and internal fixation with a Smith Peterson nail, 7 inch McLaughlin side plate and additional 8 inch slotted plate (Fig. 1, A,B). Refracture occurred 3 months later and was treated with a 3 inch hip nail and Zickel intermedullary rod with Methylmethacrylate (Fig. 1, C,D).

Case 2. Austin Moore prosthesis without Methylmethacrylate.

A 69-year-old mentally retarded female underwent a left mastectomy 10 years ago for carcinoma of the breast. Recent evaluation discovered an osteolytic lesion of the left femoral neck following 2 months of left hip pain. Despite a course of radiation therapy, a pathologic fracture of the left femur developed. Because solid intertrochanteric bone was found at surgery, the pathologic fracture of the femoral neck was treated with an Austin Moore prosthesis without Methylmethacrylate (Fig. 2, A,B). In her retarded state, the patient often maintained a flexed position of the hips in bed and on two occasions dislocated the prosthesis. Closed, and subsequently open, reduction of the prosthesis were accomplished.

Case 3. Rush rods and humeral metastases.

A 52-year-old male presented with metastasis from renal carcinoma to the choroid of the right eye.[8] Osteolytic metastasis to the right humerus became progressively more painful one and one-half years later and, despite recent radiation therapy, subsequently fractured. Treatment consisted of en-block resection of the metastatic focus and reconstruction of the proximal humerus with 2 Rush rods and Methylmethacrylate with pain relief and routine use of the right arm (Fig. 3, A,B). The patient died of metastatic malignancy one and one-half years later.

Case 4. Ritchey pins and humeral metastasis.

A 74-year-old male presented with a pathologic fracture of the right humerus secondary to well differentiated papillary adenocarcinoma of unknown origin. Successful treatment consisted of tumor excision and internal fixation with Ritchey pins and Methylmethacrylate (Fig. 4, A,B,C). Four years later the

Fig. 2, A & B. Pathologic fracture of the left femoral neck (arrows) from metastatic carcinoma of the breast was treated with an Austin Moore prosthesis without Methylmethacrylate.

patient is alive and well with a useful and painless right arm. Extensive search for a primary tumor has been unsuccessful.

Case 5. Prophylactic use of Kuntscher nail.

An 85-year-old female presented with a one month history of right thigh pain secondary to metastatic breast carcinoma following a left mastectomy in 1941 and a right mastectomy in 1958. Presumed lung matastasis had been controlled with stilbestrol therapy since 1959. Although pathologic fracture was not present, prophylactic excision of the lytic tumor of the femur with internal fixation using a Kuntscher nail and filling of the large bony defect with Methylmethacrylate was successfully accomplished (Fig. 5, A,B). Immediate results were good with painless ambulation possible at discharge.

Case 6. Mortality 12 days following surgery.

A 75-year-old male developed severe left lower extremity pain associated with an osteolytic lesion of the femur and large right posterior hilar lung mass. Needle biopsy of overlying soft tissue mass of the right thigh revealed metastatic epidermic carcinoma consistent with lung primary. A good surgical result was obtained with excisional biopsy, packing with Methylmethacrylate and internal fixation with 2 stacked 10mm and 11 mm Kuntscher rods (Fig. 6, A,B). The patient developed acute urinary retention after his hospital discharge which led to a progressive downhill course, coma, and death 30 days after the orthopedic surgery.

Case 7. Successful bilateral total hip replacements.

A 70-year-old male developed pulmonary and left hip metastases 4 months following a left nephrectomy for renal carcinoma. A pathologic fracture of the left hip was successfully treated with a Charnley Mueller total hip replacement (Fig. 7, A,B). The patient did so well that right total hip replacement was performed for long standing symptomatic degenerative arthritis (Fig. 7, B,C). Despite increasing pulmonary metastases, the patient remains asymptomatic almost 3 years following his first total hip replacement.

Case 8. Kuntscher rod for right femur metastasis. Giliberty prosthesis for left hip metastasis.

A 49-year-old female was noted to have diffuse bone metastases 1 month following mastectomy for carcinoma of the breast. Despite courses of almost every available form of chemotherapy, the patient became increasingly disabled by bone pain and subsequently developed a pathologic fracture of the right femur. Debridement of the mid femoral shaft lesion confirmed metastatic disease consistent with medullary carcinoma of the breast. Open reduction and internal fixation were accomplished with an 11 mm. and 36 cm. Kuntscher intramedullary nail and Methylmethacrylate reconstruction of the femoral shaft (Fig. 8, A,B). During hospitalization, known left hip metastasis became painfully symptomatic, and three and one-half weeks later excision of the left femoral head and neck was accomplished with insertion

Fig. 3, A & B. Pathologic fracture of the humerus from metastatic renal carcinoma (arrows A) was treated with excision of tumor, Rush rods and Methylmethacrylate (arrows B).

of a Giliberty endoprosthesis (Fig. 8, C,D). Pain relief of the right femoral and left hip metastases was accomplished, but successful ambulation was prevented by ensuing intractable back pain for lumbar vertebral metastases. The patient died 6 months later from diffuse metastatic disease.

Case 9. Modified long stemmed Giliberty prosthesis.

A 65-year-old female underwent a left mastectomy for carcinoma of the breast 7 years ago. Recent workup for right hip pain discovered a mixed osteolytic and osteoblastic metastatic process involving the entire intertrochanteric area of the right hip, associated with a subtrochanteric fracture. Curretted bone sections demonstrated metastatic adenocarcinoma consistent with breast origin, and the patient was treated with a modified Giliberty prosthesis consisting of a special long femoral stem to replace the entire upper femur. Successful stabilization was augmented wth Methylmethacrylate. (Fig. 9, A,B).

Discussion

Although a generally poor prognosis weighs heavily on patients with metastatic disease to bone, there are instances where a painful disabling metastatic deposit far outshadows the overall chances for survival. The aggressive, surgical approach toward the treatment of the isolated, painful, metastatic focus with imminent or actual pathologic fracture by local tumor resection, open reduction and internal fixation is well established. Pain relief, early joint motion, and weight bearing leading to functional ambulation, ease of nursing care and decreased cost of a shorter hospitalization, in many instances justifies orthopedic surgical intervention. The alternative is often a prolonged bedridden period of immobilization and hospitalization with the painfully uncomfortable patient unable to care for himself. In most instances, our experience with the surgical management of 9 patients with metastatic bone disease reinforces the successful national experience and establishes the orthopedic surgeon as an invaluable member of the cancer management team in the State of Maine.

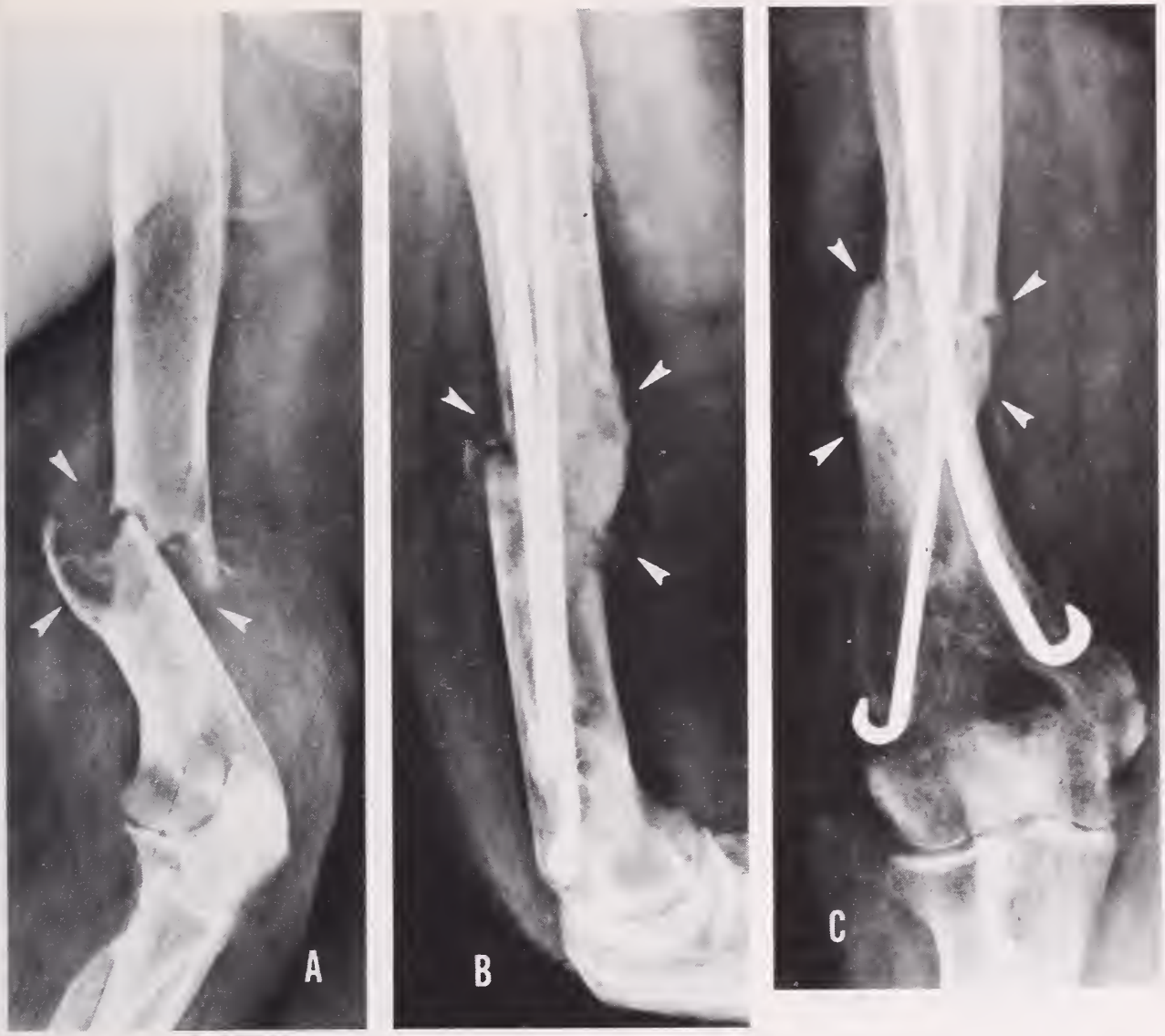


Fig. 4, A, B & C. Pathologic fracture of the humerus from adenocarcinoma of unknown origin (arrows A) treated with excision of tumor, Ritchey pins, and Methylmethacrylate (arrows B & C).

The myriad of orthopedic internal fixation and prostheses in conjunction with the rapidly stabilizing effect of Methylmethacrylate has revolutionized the management of pathologic fractures over the past 10 years.[1,6] Douglass' comparative experience with operative and nonoperative methods clearly establishes the superiority of a surgical approach. In a series of 71 pathologic fractures of long bones, 61% became ambulatory following internal fixation whereas of those treated by external fixation, (cast, splint, and traction) only 27% ever walked. Their initial experience with multiple internal fixation devices was without Methylmethacrylate but later use of the intramedullary acrylic cement became routine.[5] Although there may be instances where the metastatic process is not extensive affording solid continuous bone for internal fixation without Methylmethacrylate (Case 2, Fig. 2), internal fixation alone offers less reliable stabilization and may result in broken hardware (Case 1, Fig. 1). Harrington's treatment of pathologic fractures with local tumor resection and internal fixation supplemented by routine use of intramedullary Methylmethacrylate proved highly successful. Of 375 cases, 94% became ambulatory and 85% achieved excellent or good pain relief.[6]

Methylmethacrylate affords immediate stability. The acrylic resin rapidly polymerizes to a strength equal to adjacent bone and does not decrease fracture union or interfere with postoperative radiation. Although radiation alone is useful in control of pain in metastatic osseous disease, it does not prevent pathologic fracture (Cases 2 and 3) and may prevent fracture healing unless at least 2000 rads are used or

Fig. 5, A & B. Osteolytic metastases to the right femur (arrows A) from carcinoma of the breast treated with prophylactic excision of the more proximal tumor, Kuntscher nail and Methylmethacrylate (arrows B).

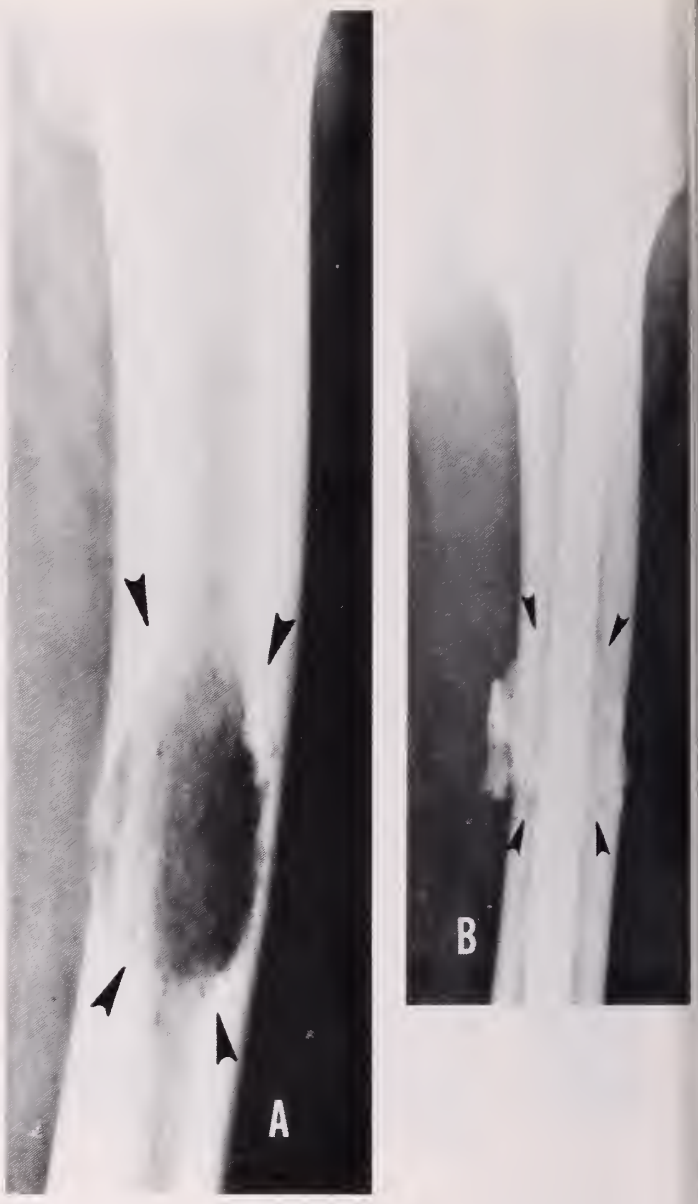
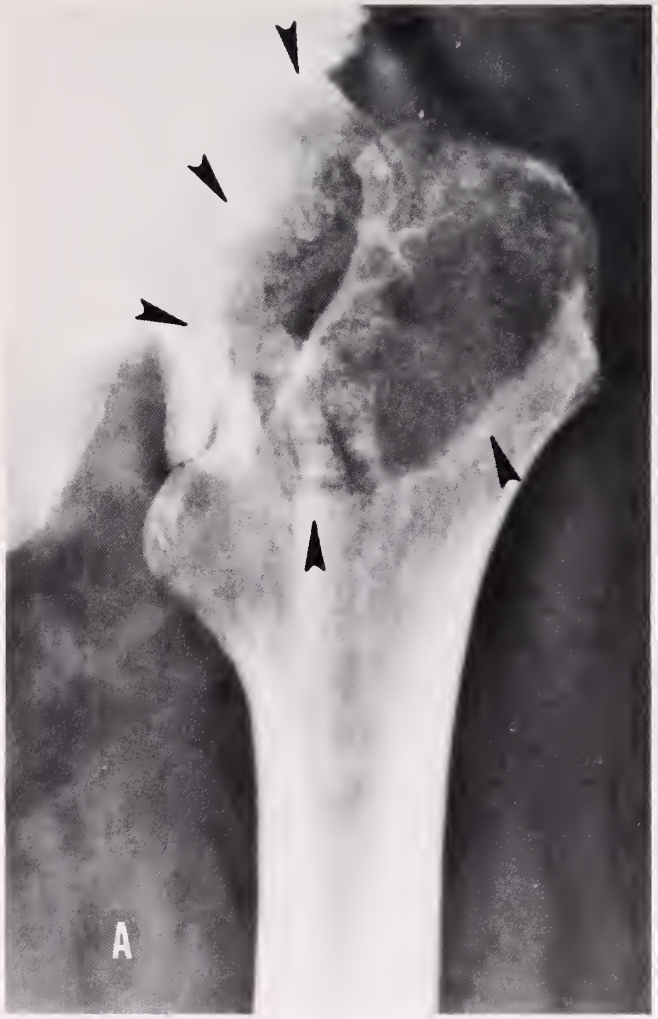


Fig. 6, A & B. Impending pathologic fracture through an osteolytic metastases (arrows A) to the right femur from carcinoma of the lung was treated with prophylactic excision of tumor, Kuntscher rod and Methylmethacrylate (arrows B).

there is rigid internal fixation. Even with painful vertebral body metastases, the traditional domain of therapeutic radiation, Methylmethacrylate is being used for stabilization and reconstruction of the destroyed vertebrum.[1] Apparently, radiation does not alter or lessen the structural properties of the resin.[1]

The choice of orthopedic applicance used for internal fixation varies from patient to patient and depends upon the site of the metastatic focus and experience of the orthopedic surgeon. Our 9 patients were treated with Rush rods, Kuntscher nails, Smith Peterson nails, Zickel rod and Ritchey pins. Prostheses included an Austin Moore, Charnley Mueller total hip and a Giliberty and modified long stemmed Giliberty endoprothesis. The use of these Giliberty protheses in 2 patients represents the very rare instance where the appliance has been utilized in metastatic disease (Cases 8 and 9) and presumably the first such use in Maine. Patients with osseous metastases often are made more comfortable with palative radiation and/or chemotherapy. It is not unusual for survival to last 6 to 12 months following the diagnosis of bone metastases. Any patient with an impending or actual pathologic fracture who is in reasonably good medical condition is considered for operative fixation. The decision for surgery is made after medical consultation and considerable discussion with the patient and members of the family. In most instances the outcome of treatment of pathologic fractures with internal fixation is favorable. The length of survival of the patient, however, is often unpredictable. Although one patient died 30



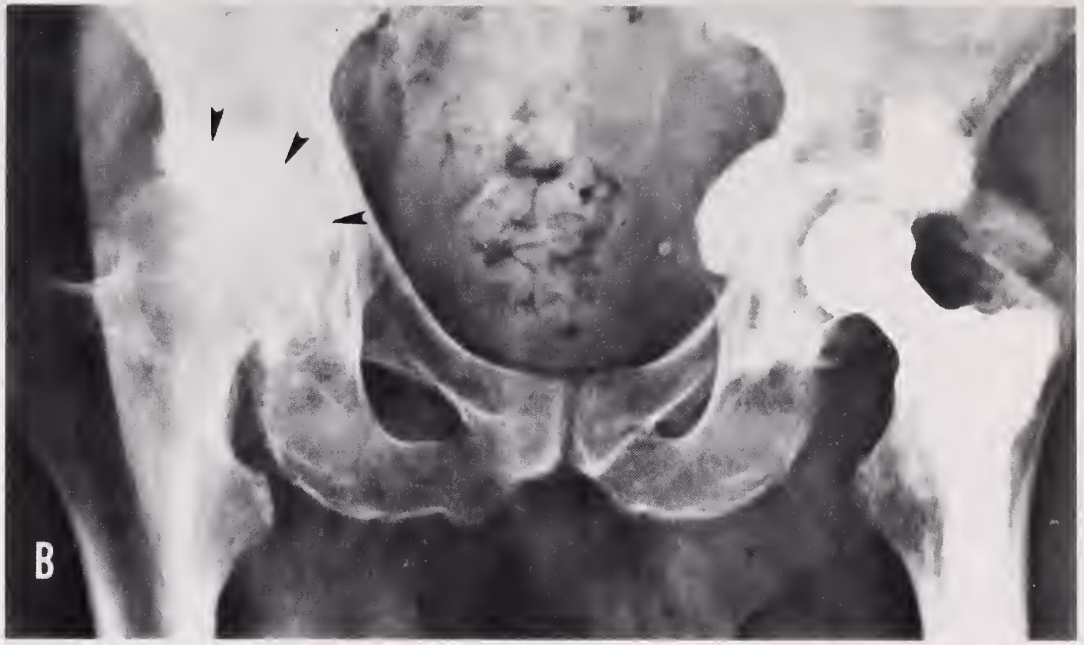


Fig. 7, A, B & C. Pathologic fracture of the left hip through large osteolytic metastases, (arrows A) from renal carcinoma treated with a total hip replacement (B). Symptomatic degenerative arthritis of the right hip (arrows B) treated with total hip replacement one year later (C).

Fig. 8, A & B. Displaced pathologic fracture of the right femur (arrows A) from carcinoma of the breast was treated with excision, Kuntscher rod and Methylmethacrylate (arrows B).

days after surgery (Case 6), and another patient developed painful vertebral metastases which limited ambulation (Case 8), all seven other patients were discharged from the hospital ambulatory with or without a walker with good pain relief. Four patients have died from their disease; two were lost to follow up; the remaining three patients are alive up to four years after orthopedic surgery and are asymptomatic despite other known sites of metastasis in 2 of these patients. Extremely good outcome is present in Case 7 who did so well that he underwent a total right hip replacement for benign degenerative arthritis following a total left hip replacement for metastatic disease. In another patient we have been unable to find a primary tumor. He is alive and well 4 years after surgery without evidence of other metastatic deposits (Case 4).

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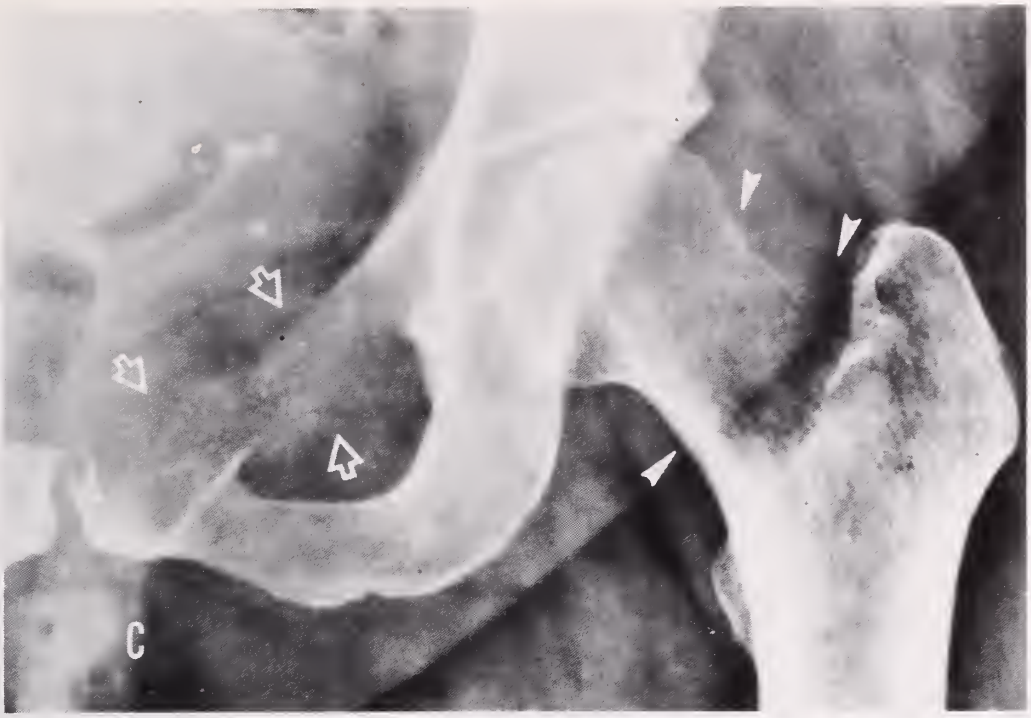

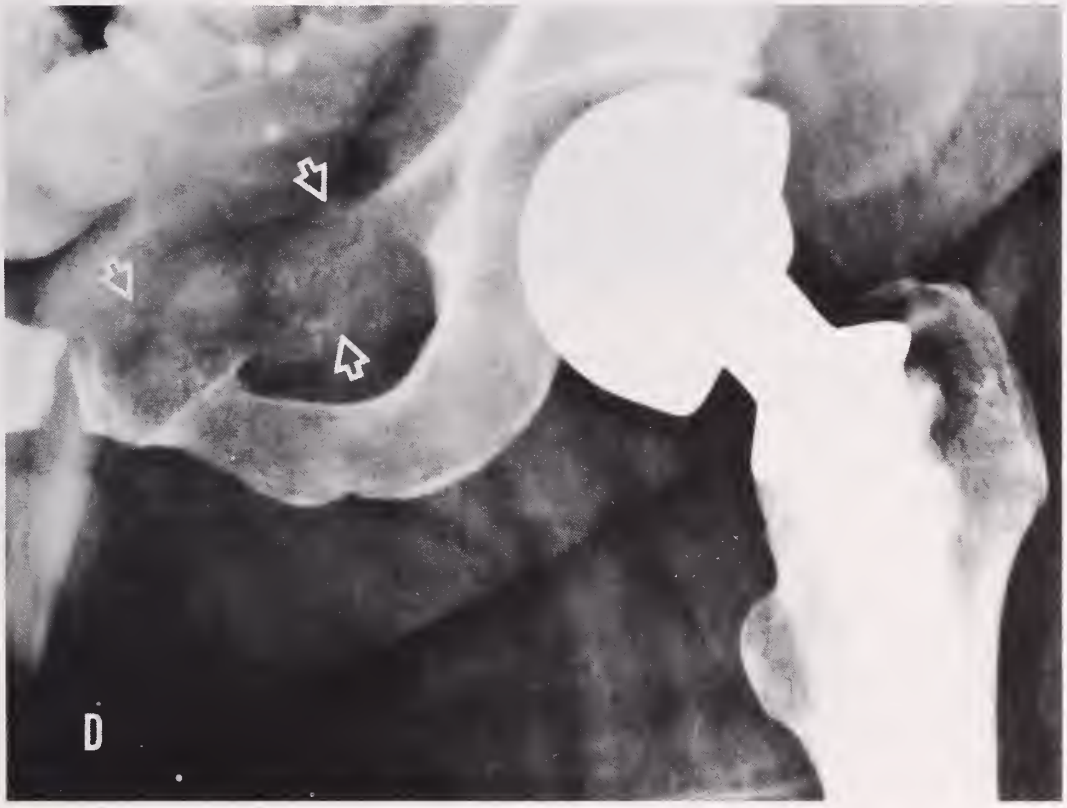

Fig. 8, C & D. Impending pathologic fracture of extensive osteolytic metastases to the left femoral neck (arrows C) was treated with Giliberty prothesis (D). Note osteolytic metastases to the superior pubic ramus also (open arrows C & D).

Fig. 9, A & B. Subtrochanteric fracture of the right hip through extensive bone destruction (arrows A) from metastatic breast carcinoma was treated with a modified, long stemmed Giliberty prosthesis and Methylmethacrylate to replace the upper femur (B).

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The Spigelian Hernia

CHARLES H. STONE, III, M.D.

During the past four years, four patients have been examined because of severe abdominal pain, thought by the patient or the referring physician to be caused by acute abdominal disease (e.g., appendicitis or cholecystitis.) In each instance, a spigelian hernia was diagnosed. One fifty-year-old patient had undergone extensive diagnostic work-up for upper gastrointestinal disease at one of our large medical centers in Maine, as well as extensive evaluation in Boston for possible coronary-artery insufficiency. Since repair of her "spigelian" hernia, the patient has been free of all symptoms for over two years. Prior to that she had pain almost constantly.

Adriaan van der Spieghel (1578-1625) was professor of anatomy, Padua. It was he who described the linea semilunaris which marks the junction of the transversus abdominis and internal oblique aponeurosis at the lateral border of the rectus abdominis muscle. The line extends from the costal margin to the symphysis pubis. Spigelian hernias occur anywhere along this line. The hernia is usually quite small and does not penetrate the external oblique aponeurosis or fascia. It is usually at the site of penetration of a small vascular bundle, and when small, consists only of pre-peritoneal fat. In an obese patient, no mass may be palpable. In his text, "Abdominal Operations," Rodney Maingot devotes five paragraphs to this entity and states that about two hundred cases have been reported in the world literature. Because these hernias are small, and because they may be in an "unusual" location, they are often missed. Patients may be subjected to extensive and expensive investigation before someone finally suspects and then finds the hernia. One important physical sign is that pain on palpation is made worse by tensing the abdominal musculature. In patients with underlying peritoneal irritation, tensing of the abdominal musculature will relieve the pain produced by palpation. Another important physical sign is almost pin-point tenderness at the site of the hernia. Palpation at this point with one finger will exacerbate the patient's pain.

Surgical treatment of this unusual hernia is simple and provides immediate relief of the often perplexing symptoms.

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Box 498, Greenville, Maine 04441

Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The Maine Medical Association's House of Delegates, at its June 1976 meeting, adopted a regulation stating that a *minimum of 150* hours of continuing medical education is required in order to maintain membership. The policy took effect on January 1, 1977 and all members must be certified by January 1, 1980. Eligibility for certification begins January 1, 1977.

Credits required for the three-year period are as follows:

Category 1 — CME Activities with Accredited Sponsorship **(60 hours required)**	**No limit**
Category 2 — CME Activities with Non-accredited Sponsorship	**45 hours**
Category 3 — Medical Teaching	**45 hours**
Category 4 — Papers, Publications, Book and Exhibits	**40 hours**
Category 5 — Non-supervised individual CME Activities	**45 hours**
Category 6 — Other Meritorious Learning Experience	**45 hours**

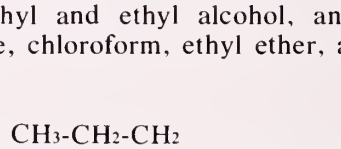
Only active, dues-paying members are required to report. Please fill in your activity report promptly and return to the M.M.A. office, P. O. Box 250, Brunswick, Maine 04011.

A Brief Review of Valproate

A New Anticonvulsant

WILLIAM H. AUSTIN, M.D. AND HERBERT E. THORNE, JR., M.S.

Sodium valproate, the sodium salt of isopropyl acetic acid, was first synthesized over 100 years ago. Chemically, it is sodium 2-propylpentanoate, and has a molecular weight of 166.2. It has been known chemically by other terms such as sodium Depa, sodium dipropylacetate, sodium 2-propylalerate, and other variations. It will be marketed by Abbott Laboratories with a proprietary name of Depakene, but has yet to be released for general use. In reviewing the literature, we found it was identified by other proprietary names such as Eurekene, Epilim, Eigenyl, Labazene, and Depakin. It is of interest that unlike other anticonvulsants, valproate has no ring structure nor nitrogen atoms, as may be seen by the formula. It is water soluble, and a 5% aqueous solution yields a pH of from 7 to 8. It is very soluble in methyl and ethyl alcohol, and insoluble in acetone, chloroform, ethyl ether, as well as benzene.



Formula for sodium valproate

The usual dose in adult patients appears to be from 500 to 1000 mg. per day in divided doses, and toxic doses are in the range of from 35 to 40 Gm. per day. Since it is rapidly absorbed, gastric lavage is of limited value in treatment of overdose, and we find no studies relating to its dialyzability.

When administered orally, it reaches peak blood levels in 1 to 4 hours, and, on an empty stomach, is converted to dipropylacetic acid, which may cause gastric irritation.[1] For this reason, administration with milk is advisable, and it may be taken in this way without adversely affecting the blood levels. If given after a meal, the peak blood level is delayed; however, total absorption is complete. Studies state that stable blood levels are achieved in approximately 24 hours, and the half-life of the drug is 7 to 8 hours, although this figure has not been documented.

The concomitant admission of Dilantin® (phenytoin), Mysoline® (primidone), phenobarbital, and Tegretol® (carbamazepine) do not seem to alter the half-life to any great extent.[2] Statements have been made that these drugs do actually shorten the half-life due to activation of hepatic enzymes; however, this impression is gained from the fact that if sodium valproate is used over a protracted period the half-life is prolonged. The blood levels, according to some studies,[3,4] range in the therapeutic level of from 40 to 70 or to 80 mcg/ml. Generally, it is considered that the therapeutic levels are from 50 to 100 mcg/ml, since most patients with levels in this range are controlled satisfactorily when the drug is effective. As with other anticonvulsants, there are difficulties in relating blood levels to the therapeutic responses, and at this time it does not appear that blood levels will be an extremely effective tool in the use of this drug clinically.[5] Sodium valproate is excreted in the saliva; however, the levels correlate poorly with those in the plasma, unlike other anticonvulsants, making monitoring unsatisfactory.[6] Once absorbed, sodium valproate is distributed very rapidly to the circulating plasma and to the exchangeable extracellular water. It reaches concentrations in the brain quickly; however, only approximately one-tenth of those levels are achieved in the serum. This is consistent with the finding that spinal fluid levels are achieved by valproate at only one-tenth of the levels achieved in the serum.[3] There does not appear to be a homogeneous distribution of the drug in the cerebellum; however, it is probably greater than in the cortex. There are several analogues of valproate (2,2-dipropyl ethanol, and 2,2-dipropyl ethyl ester) which, while having anticonvulsant properties, are more toxic. The glycerol tripropylacetate seems to be a form of dipropylacetate which may have some clinical application. The depramide of dipropylacetic acid also is an active moiety which as a half-life of almost twice that of the acid form.[1]

The fate of this compound is not known with certainty. Plasma protein binding is apparent, and disodium valproate is strongly bound to plasma (90%). Only 60% of this is bound to albumin, and the percentage of "free" form has been found to be approximately 10%.[7] It is of interest to note that valproate may displace phenobarbital from its protein binding site. The drug is excreted in the kidneys intact, in only a small amount, and is probably metabolized in the liver. Tagged portions of radioactive valproate will subsequently distribute themselves in the blood, gallbladder, kidney, liver and eventually even in the small intestine, urinary bladder and nasal septum.[8] Almost all of the radioactivity has left the body, and the major concentration of the isotope is found in the urinary bladder, which suggests that the metabolites of sodium valproate are excreted renally, although the degradation is primarily in the liver. At this time, it is safe to say that the mechanism of action of sodium valproate itself is not well known, but the elevation of glutamic

aminobuteric acid has been correlated with the anticonvulsant effect of sodium valproate. Seizures, therefore, may result from an inability of the formation of aminobuteric acid or enzymes responsible for its synthesis. One can speculate that sodium valproate may take the place of gamma aminobuteric acid in its inhibitory role at the synaptic junction. Again, from the information we were able to obtain, this is all speculative, and certainly further work will clarify this point.

There have been conflicting reports as to the effectiveness of this anticonvulsant in different types of seizures. One of the problems is that there have been discrepancies in the classification of different seizure types, and many individuals who have severe intractable seizures are already taking anticonvulsants, and the primary effect of a valproate compound may be modified by these.

For practical purposes, a simple listing of seizures is made: *1.* Tonic-Clonic, *2.* Absence, *3.* Myoclonic, *4.* Akinetic (including atonic) and, *5.* Partial seizures, with sub-groups of Elemental and Complex. The remaining seizure types are grouped under the heading of Mixed Seizures.

The majority of this information is abstracted from the work of Pinder[7] and Simons.[9] Although the groups studied varied greatly in size, the results were surprisingly similar. The overall response of over two thousand patients studied showed that slightly over forty-five percent of these patients demonstrated a drop of seventy-five percent or more from their previous seizure rate. Twenty-five percent of the group experienced drops in seizure rates of from thirty-five to seventy-five percent, and the remaining twenty-five percent of the group had no significant change in seizure activity.

By seizure type, tonic-clonic response to valproate was 50% good to excellent, 20% fair, with the balance poor. Absence seizures responded with 75% good to excellent, 10% fair, and the balance poor. Myoclonic seizures showed 75% with a good to excellent response, with the balance equally divided between good and fair and poor. Akinetic seizures responded with 30% in the good to excellent range, 20% in the fair to good range, and the remaining 50% with no change. Partial seizures with complex symptomatology were difficult to assess, but showed generally a 25% response in the good to excellent range, 30% good to fair and 45% poor. Partial seizures with elementary symptomatology produced figures of 25%, 50%, and 25% respectively.

Obviously these figures will vary from other data; however, they represent rough figures which we estimated from the literature available. We take exception to the November 18th issue of *The Medical Newsletter* which suggests serious side effects from sodium valproate. The objectivity of their report is questionable since they did not acknowledge the role of other agents as contributing or primary factors.

Nonetheless, there is information to indicate that platelet function is adversely affected in a small number of patients. For this reason, the drug should not be used in conjunction with aspirin or anticoagulents of any type. Also it has been suggested that clonazapam (Clonopin®) should not be used in conjunction with sodium valproate or any of its analogues. The combination may precipitate petit mal status. Since sodium valproate is partially eliminated by the kidney, in the form of ketones, false-positives for ketone bodies may result in testing diabetic urine.

Summary

In conclusion, it appears that sodium valproate and/or its analogues is a promising anticonvulsant. Our personal experience with retarded patients tends to bear this out. However, we do not have significant experience to make statistically sound statements.

Addendum

Since the completion of this manuscript, valproate has been released by the FDA in the form of valproic acid. It is marketed in capsules of 250 mg which can not be broken, as it is in a liquid state. The usual starting dose is 250 mg three times daily, and in the phase III studies for the FDA it was suggested that the dose be increased in increments of 250 mg. The fact that it is in the acid form does not make any practical difference. However, as noted above, most studies have been done using sodium valproate.

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Clinical Pharmacology of Antiepileptic Drugs

THOMAS R. BROWNE, M.D.

ABSTRACT

The absorption, distribution, biotransformation, excretion, and clinical pharmacokinetics of antiepileptic drugs are reviewed, and six guidelines are stated. (1) When therapy with an antiepileptic drug is initiated or when dosage is raised or lowered, the new steady-state drug serum concentration and the full effect of the dosage change will not occur for five elimination half-lives. (2) A loading dose is usually necessary to immediately achieve a steady-state serum drug concentration equal to the usual maintenance steady-state serum drug concentration. (3) The choice of dosage intervals for antiepileptic drugs is determined in part by the range of fluctuation in drug concentration between doses that is acceptable. (4) Addition of a drug to an existing antiepileptic regimen may raise or lower the serum concentration of prior drugs by inhibition or induction of their metabolism. (5) If possible, make only one change at a time in an antiepileptic drug regimen. (6) Antiepileptic drugs should not be given by the intramuscular route in emergency situations.

This paper will review the absorption, distribution, biotransformation, and excretion of antiepileptic drugs. This will be followed by a discussion of how pharmacokinetic principles can be applied to the administration of antiepileptic drugs and a summary of the pharmacokinetic parameters of the frequently prescribed antiepileptic drugs.

ABSORPTION

Basic Principles

Drugs that are used to treat disorders of the central nervous system ideally should be both water and lipid soluble — a characteristic that, unfortunately, is physically impossible. Water solubility permits preparation of aqueous solutions for injection and rapid dissolution of tablets or capsules in the gastrointestinal tract. Lipid solubility permits rapid passage of the drug into the brain parenchyma. Most antiepileptic drugs are weak acids or weak bases and thus exist as a mixture of ionized (more water-soluble) and non-ionized (more lipid-soluble) molecules. Changing the pH of the biological fluid or liquid in which a drug is dissolved changes the percentage of a drug that is ionized and its relative water and lipid solubilities.

Phenytoin illustrates the importance of these concepts. It is a weak acid with a pK_a of approximately 9.0.[1] At a pH of 1 to 2, phenytoin is less than 1% ionized and has a water solubility of about 14 μg/ml. At a pH of 7.5, phenytoin is 3% ionized and has a water solubility of 100 μg/ml. Thus, little phenytoin is absorbed in the stomach, and phenytoin absorption takes place largely in the small intestine. At pH 9.0, phenytoin is 50% ionized and has a water solubility of 165 μg/ml. In order to dissolve phenytoin in a small volume of liquid for parenteral administration, a solution with a pH of 12 is prepared. When this preparation is injected intramuscularly (i.e., into a medium with a pH of about 7.4), the water solubility of the drug decreases significantly, phenytoin crystals precipitate in the muscle,[2,3] and the drug is absorbed very slowly.[4,5]

Intramuscular Route

Peak serum phenytoin concentrations occur approximately 24 hours after a single intramuscular injection and are significantly less than the peak levels produced by the same dose given by rapid intravenous infusion.[5] Peak phenobarbital and diazepam concentrations are reached in 1 to 12 hours[6,7] and 45 to 60 minutes,[8-10] respectively, after intramuscular injection. Peak diazepam serum concentrations after intramuscular injection also are significantly less than the peak concentrations produced by the same dose given by rapid intravenous infusion.[8] Antiepileptic drugs should not be given via the intramuscular route in emergency situations (e.g., status epilepticus) because of slowness of absorption and relatively low peak serum concentrations.

The use of the intramuscular route for administration of maintenance doses of antiepileptic drugs remains controversial. Potential problems have been reviewed elsewhere.[11] Eventually, almost all of an intramuscular injection of phenytoin is absorbed, and regimens for administration of maintenance

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doses of intramuscular phenytoin have been published.[12,13] However, peak phenytoin serum concentrations occur 24 hours after an intramuscular injection[5] and are variable. Further, serum concentrations may fall below therapeutic levels shortly after switching to the intramuscular route from the oral or intravenous route and may ascend into the toxic range because of accumulation after switching back from the intramuscular to the oral route.[2,3,12,14] Intramuscular phenobarbital and diazepam are slowly absorbed (see above), and the absolute systemic availability of these drugs by this route is not known. In most situations, maintenance doses of antiepileptic drugs should not be given by the intramuscular route because of the slowness and variability of absorption and because of the danger of over-medication and under-medication when switching to and from other routes of administration.

Oral Route

Different oral preparations of the same generic drug may have different bioavailability. For example, significant differences in peak serum concentrations and bioavailability have been reported following oral administration of the same dosage of phenytoin capsules supplied by different manufacturers.[15-18] Increased seizure frequency[19] and increased drug toxicity[20,21] have been reported when the brand of phenytoin capsule used by a group of patients was changed. When prescribing an antiepileptic drug available from several manufacturers, one product should be routinely used.

Phenytoin oral suspension has significantly greater bioavailability than many capsule preparations.[17] Patients who do not absorb phenytoin capsules well may have a significant increase in serum phenytoin concentration when they are given the same dose in an oral suspension. Phenytoin oral suspension must be shaken well before each dose to prevent the drug from "settling out" in the bottom of the bottle, resulting in under-medication with suspension taken from the top of the bottle and over-medication with suspension from the bottom of the bottle.

Distribution

Route of Administration

After administration of an antiepileptic drug by the *oral* or *intramuscular* route a rise and then a fall in serum concentration occurs. The rates of rise and fall depend on the rates of absorption, distribution, and elimination of the drug.[22,23] After *intravenous* administration of a drug, a similar time-drug concentration curve is observed, except that higher peak concentrations are achieved more quickly and the decline from the peak occurs more rapidly. The rapid decline occurs as the drug distributes into various tissues.[22,23] A second phase of slowly declining serum concentrations follows, and it corresponds to the elimination of the drug by the processes of biotransformation and excretion.[22,23] Phenytoin[24-26] and diazepam[27,28] demonstrate this type of "biphasic" fall in serum concentration after intravenous administration. The pharmacokinetics of intravenous phenobarbital have not been extensively studied. The half-life of fall of serum concentration during the "distribution" phase after intravenous injection is 0.38 to 1.23 hours for phenytoin[25] and 15 to 60 minutes for diazepam.[27,28] When administering a loading dose of intravenous phenytoin, the dose should be sufficiently large to ensure therapeutic serum concentrations after the rapid fall in serum concentration during the distribution phase (see below). The rapid fall in serum diazepam concentration following an intravenous injection may account for the observation that status epilepticus not infrequently recurs after a single intravenous injection of diazepam if a long-acting, less rapidly distributed, antiepileptic drug is not also given.

Distribution to Active Site

Antiepileptic drugs presumably exert their action on neurons and/or glial cells of the central nervous system. In order to enter these cells, the drug molecules must pass the blood-brain barrier and the cell membrane. The rate of penetration of brain cells by antiepileptic drug depends on lipid solubility and other factors, and varies among the antiepileptic drugs. The concentration of phenytoin in the brain parenchyma and cerebrospinal fluid (CSF) may not reach peak levels until an hour or more after an intravenous injection in man.[26] However, animal work indicates that the brain parenchyma concentration of phenytoin remains greater than the serum concentration once peak brain concentrations are reached,[29] presumably because of binding by brain cells. The rate at which intravenously-administered phenobarbital enters the brain in man has not been studied. However, the relatively slow onset of hypnosis following intravenous phenobarbital in man suggests that the drug probably enters the brain relatively slowly. Diazepam very rapidly enters the brain parenchyma of animals, and brain concentrations of diazepam closely parallel serum concentrations.[29] Thus, the brain concentration of diazepam peaks soon after an intravenous injection but falls rapidly in association with the rapidly falling serum concentration (see above). These observations provide a partial basis for the therapeutic strategy of treating status epilepticus with a single dose of intravenous diazepam (to quickly stop the seizures) followed immediately with a loading dose of phenytoin to provide long-term antiepileptic activity.

Protein Binding

Upon entering the blood stream, antiepileptic drugs are bound to differing degrees by plasma proteins, primarily albumin. The extent of protein binding by various antiepileptic drugs is listed in Table 1.

Table 1

Pharmacologic Data on Five Antiepileptic Drugs

Drug	Elimination half-life (hr)	Time to reach steady-state (days)	Therapeutic serum concentrations (μg/ml)	Protein binding (%)	References
Phenytoin	10 to 34[a]	7 to 8	10 to 20	69 to 96	1, 30-39
Phenobarbital	56 to 136	14 to 21	15 to 40	40 to 60	40-43
Primidone[b]	6 to 18	4 to 7	5 to 12	0	43, 44
Carbamazepine	14 to 27[a]	3 to 4	4 to 12	70 to 86	45-52
Ethosuximide	20 to 60	7 to 10	40 to 100	0	53-60

a: May be less in children (61, 62).
b: Primidone is metabolized to phenobarbital and phenylethylmalonamide. Both these derivatives have antiepileptic activity.

Protein binding has several important clinical implications. First, drug assays done by most laboratories measure the total (bound and unbound) and not the free (unbound) drug serum concentration. Second, only free drug can enter active sites from the plasma, and there is some evidence that the unbound serum concentration correlates better with efficacy and toxicity than does the total concentration.[63] Third, the percentage of free drug in the serum is inversely proportional to the albumin concentration. Patients with low plasma albumin concentrations have more unbound antiepileptic drug (and a greater probability of developing antiepileptic drug toxicity) for a given total drug serum concentration than do patients with a high plasma albumin concentration.[38,64,65] Fourth, other concurrently administered drugs may displace the antiepileptic drug from its protein binding sites, resulting in a higher percentage of free antiepileptic drug.[1,35,38,66] The available evidence indicates that coadministration of other antiepileptic drugs probably does not significantly alter the protein binding of phenytoin[35] or carbamazepine.[47]

Cell Storage

The concentration of free drug is usually similar in cells and serum. However, the total concentration of drug can be much higher in cells than in serum if the drug is bound by cellular components (proteins, nucleoproteins, phospholipids). As noted above, the concentration of some drugs is greater in the brain parenchyma than in the serum. Because antiepileptic drugs generally are lipid-soluble, high concentrations may accumulate in fat and other cells.[1]

Transcellular Fluids: CSF and Saliva

CSF may be viewed as a plasma filtrate with a low protein concentration (and hence little protein binding). Concentrations of phenytoin,[1,36] phenobarbital,[41] primidone,[43] carbamazepine,[45] and ethosuximide[56] in CSF are essentially identical to free drug levels in serum. Similar considerations apply to saliva, and the possibility that concentration of antiepileptic drugs in saliva might be routinely determined as a means of determining the concentration of free drug in the serum is being investigated.[67]

Biotransformation

Most antiepileptic drugs are inactivated by the mixed function oxidase system (cytochrome P-450 system) located in hepatic microsomes. This enzyme system has a low substrate specificity and metabolizes many drugs. Since several antiepileptic drugs are often given to the same patient, their common metabolism by the mixed function oxidase system may result in at least two types of clinically important drug interactions. Some antiepileptic drugs have a relatively high affinity for the mixed function oxidase system and may competitively inhibit the metabolism of other drugs given simultaneously. Other antiepileptic drugs may stimulate the mixed function oxidase system (enzyme induction) and increase the rate of metabolism of other drugs given simultaneously.

Table 2 summarizes published data on observed interactions involving antiepileptic drugs. Enzyme induction is the presumed mechanism for decreases in serum concentration of the first administered drug, and the inhibition of hepatic metabolism is the presumed mechanism for increases in serum concentration. Alterations in absorption, distribution, or excretion may also account for some of the effects listed in Table 2. The data in Table 2 are from small and sometimes conflicting studies.

Antiepileptic drugs may also influence the metabolism of other drugs and vice versa. These drug interactions have been reviewed elsewhere.[66]

The rates of biotransformation of drugs may change with age. Many drugs are slowly metabolized by the neonate because of immature hepatic microsomes. Younger children metabolize phenytoin more rapidly than do older children and adults, require higher mg/kg doses of phenytoin to achieve a given serum concentration, and sometimes cannot maintain therapeutic serum concentrations with once daily administration.[61,69,86-88]

Elimination (Combined Processes of Biotransformation and Excretion)

General Principles

Most antiepileptic drugs are inactivated by biotransformation in the liver, and the metabolic products are subsequently excreted by the kidney. Phenytoin,[1] phenobarbital[89] and ethosuximide[54] first

TABLE 2

EFFECT OF ADDING A SECOND ANTIEPILEPTIC DRUG ON SERUM CONCENTRATION OF FIRST ANTIEPILEPTIC DRUG

Original drug	*Added drug*	*Effect of added drug on serum concentration of original drug*	*References*
Phenytoin	Phenobarbital	Decrease, increase, or no change	68-73
	Primidone	No change	69
	Carbamazepine	No change	45, 71, 74
	Ethosuximide	No change	71
	Clonazepam	Data conflicting	75-77
Phenobarbital	Phenytoin	Increase	78
	Carbamazepine	No change	45
	Clonazepam	Data conflicting	76, 77
Primidone	Phenytoin	Increase in concentration of derived phenobarbital	73, 79-81
	Ethosuximide	No change	81
	Clonazepam	No change	77
Carbamazepine	Phenytoin	Decrease	45, 82-84
	Phenobarbital	Decrease	45, 82-84
	Primidone	Decrease	84
Clonazepam	Phenytoin	Decrease	85
	Phenobarbital	Decrease	77

undergo an oxidation reaction and then are excreted partly as the oxidized metabolite and partly as the conjugated oxidized metabolite. The initial oxidation step renders these drugs inactive as antiepileptic drugs. Primidone is oxidized to two active metabolites, phenobarbital and phenylethylmalonamide.[43] The derived phenobarbital is then metabolized and excreted as described above. Carbamazepine may undergo oxidation to form carbamazepine-10,11-epoxide or carbamazepine-10,11-dihydroxide.[50] Carbamazepine may also undergo loss of the carbamide group to form iminostilbene.[50,90] Carbamazepine-10,11-dihydroxide has antiepileptic activity.[90] Diazepam is demethylated to form desmethyldiazepam, then oxidized by hydroxylation to form oxazepam.[91] Both these metabolic products possess antiepileptic activity, although only desmethyldiazepam accumulates in blood to a significant degree. The major excretion product is oxazepam glucuronide, a water-soluble pharmacologically inactive metabolite.

Effect of Hepatic Failure

In patients with hepatic disease, the rate of inactivation and/or conversion to active metabolites of antiepileptic drugs is slowed. Unfortunately no method is available for predicting the proper dose of an antiepileptic drug based on liver function tests. Drug dosage must be adjusted on the basis of frequent determinations of serum drug concentration.

Effect of Renal Failure

In patients with renal failure and no impairment of liver function, hepatic biotransformation continues but renal excretion of metabolites is slowed. Uremic patients receiving phenytoin have been shown to have lower serum phenytoin concentrations, higher HPPH (hydroxyphenyl-phenylhydantoin, the principal metabolite of phenytoin) concentrations, and *shorter* phenytoin elimination half-lives than nonuremic patients receiving the same dosage of phenytoin.[92-94] The high concentrations of HPPH is presumably due to impaired renal excretion of the metabolite.The short plasma elimination half-life of phenytoin is probably due to increased accessibility of phenytoin to hepatic biotransformation enzymes due to low serum albumin concentration (decreased protein binding) and/or displacement of phenytoin from protein binding sites by HPPH. The low serum phenytoin concentration is presumably due to low serum albumin concentration and/or an increased rate of hepatic biotransformation.

PHARMACOKINETICS

Definitions

Pharmacokinetics is the quantitative study of the combined processes of drug absorption, distribution, biotransformation, and excretion to produce mathematical models that predict the concentration of a drug in various parts of the body as a function of dosage, route of administration, and time after administration.[22] Recently developed knowledge of basic pharmacokinetic principles[22,23,95] has made it possible to administer antiepileptic drugs in a safer and more effective manner. Pharmacokinetic principles can be applied to the administration of antiepileptic drugs, but before these principles are reviewed, certain terms must be defined.

First-order enzyme kinetics. In first-order enzyme processes (e.g., many biotransformation reactions), the rate of the reaction varies directly with the concentration of the drug. This can be expressed mathematically as: $dC/dt = -kC$ where C is the concentration of drug, t is time, and k is a constant quantity ("rate constant"). This type of reaction is observed in enzyme systems that are not saturable.

Zero-order enzyme kinetics. In zero-order processes, the rate of the reaction is the same regardless of drug concentration. This can be expressed mathematically as $dC/dt = -k$. This type of reaction is observed in enzyme systems that are saturable.

With first-order elimination kinetics, the steady-

state serum concentration of a drug increases proportionally with increasing dosage while the elimination half-life remains constant. With zero-order elimination kinetics, the enzymes responsible for elimination of the drug are saturated, the concentration of drug increases disproportionately with increases in dosage, and the apparent elimination half-life increases with increasing dosage.

These considerations are particularly important in the case of phenytoin. Recent pharmacokinetic studies indicate that the human body can eliminate only 3.8 to 31.8 mg/kg/day of phenytoin, and that for most persons the maximum rate of elimination of phenytoin is 4 to 12 mg/kg/day.[96-101] With doses up to this amount, there is a proportional increase in phenytoin serum concentration with increasing dosage, and the elimination half-life remains constant at about 24 hours (i.e., first-order kinetics). When the dosage exceeds 4 to 12 mg/kg/day, a small increase in dosage may produce a large increase in phenytoin serum concentration, an increase in apparent elimination half-life, and unexpected drug toxicity.[102] This phenomenon is presumably due to saturation of the enzyme system which eliminates phenytoin and a switch from first-order to zero-order kinetics.[100,103]

Compartments. Compartments are fictitious, non-anatomical volumes into which drugs are assumed to be taken up after administration. The simplest pharmacokinetic model is the one compartment model which views the body as a single compartment with only two unit processes — absorption and elimination (i.e., biotransformation plus excretion). Distribution is assumed to be uniform in all body tissues and to occur rapidly relative to absorption and elimination. This simple model often predicts well the clinical pharmacokinetics of antiepileptic drugs during chronic oral administration. A more complex two (or more) compartment model is usually necessary to predict the pharmacokinetics of single doses of a drug because of the dramatic changes in drug concentration in body tissues which occur during distribution.[22]

"Therapeutic range" of serum concentration. The lower limit of the therapeutic range of serum concentration of antiepileptic drugs is usually defined as the serum concentration below which a majority of patients fail to have a significant reduction in seizure frequency. The upper limit of the therapeutic range of serum concentration is usually defined as the serum concentration above which a majority of patients develop disturbing signs or symptoms of intoxication. Published therapeutic ranges of serum concentration of antiepileptic drugs thus represent values indicative of the majority but not all patients (Table 1). Some patients may have good therapeutic responses with serum concentrations below the lower limit of the therapeutic range,[104] while others may become toxic with serum concentrations within the therapeutic range. Other

Continued on Page 234

Tablets
Percodan® CII

DESCRIPTION Each yellow, scored tablet contains 4.50 mg. oxycodone HCl (WARNING: May be habit forming), 0.38 mg. oxycodone terephthalate (WARNING: May be habit forming), 224 mg. aspirin, 160 mg. phenacetin, and 32 mg. caffeine.

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone, aspirin, phenacetin or caffeine.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCODAN®, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCODAN® is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCODAN® should be cautioned accordingly.

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCODAN® may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCODAN® should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCODAN® should not be administered to children.

Salicylates should be used with caution in the presence of peptic ulcer or coagulation abnormalities.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions The administration of PERCODAN® or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients PERCODAN® should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

Phenacetin has been reported to damage the kidneys when taken in excessive amounts for a long time.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient. The usual adult dose is one tablet every 6 hours as needed for pain.

DRUG INTERACTIONS The CNS depressant effects of PERCODAN® may be additive with that of other CNS depressants. See WARNINGS.

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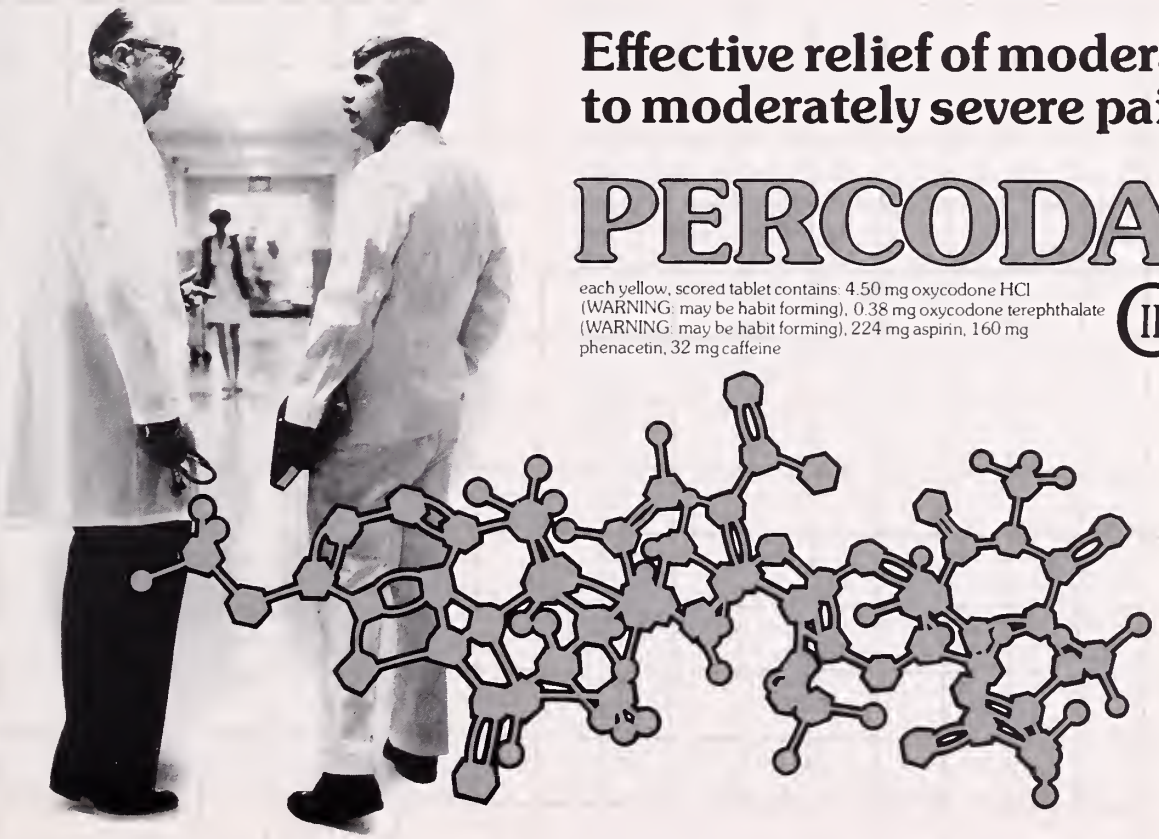

Effective relief of moderate to moderately severe pain

Tablets

PERCODAN®

each yellow, scored tablet contains: 4.50 mg oxycodone HCl (WARNING: may be habit forming), 0.38 mg oxycodone terephthalate (WARNING: may be habit forming), 224 mg aspirin, 160 mg phenacetin, 32 mg caffeine

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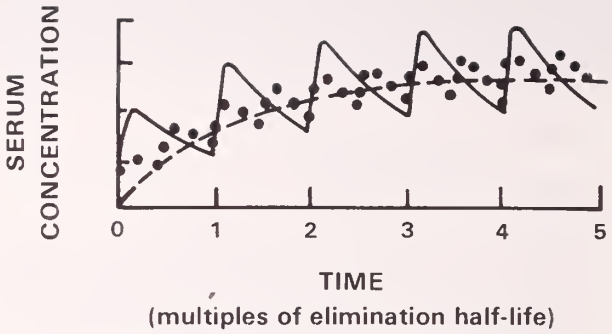

Fig. 1. Fundamental pharmacokinetic relationships predicted by one compartment model with first-order elimination kinetics. Inset table indicates the percentage of completion of elimination or build-up to steady-state concentration after multiples of drug's elimination half-life.

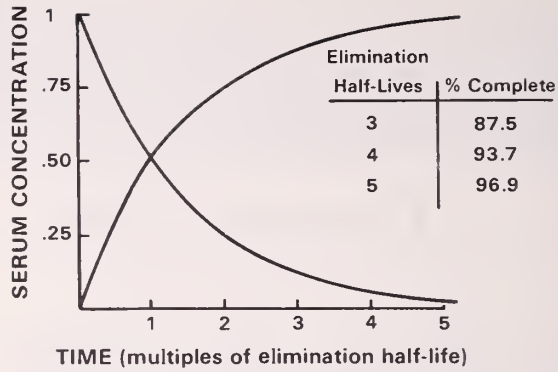

Fig. 2. Predicted kinetic patterns when the same dose per unit time of a drug is given by constant intravenous infusion (dashed line), at intervals equal to the elimination half-life (solid line), and at intervals equal to one-half the elimination half-life (dotted line). Modified from Greenblatt and Koch-Weser[22] with permission of the publisher.

patients may require serum concentrations above the therapeutic range for seizure control and exhibit no signs or symptoms of intoxication.

Clinical Pharmacokinetics

Fundamental relationships. Figure 1 describes the fundamental pharmacokinetic relationships predicted by the one compartment model assuming first-order elimination kinetics. When a drug is stopped, the concentration of the drug in the serum decreases exponentially such that after one elimination half-life the concentration of the drug has decreased by 50%, and after five elimination half-lives the concentration of the drug has decreased by more than 95%.

Many practitioners are not aware of the converse relationship illustrated in Figure 1. When a constant intravenous infusion of a drug is begun, concentration of the drug in the serum will accumulate at a rate which is the reciprocal of its rate of elimination. After one elimination half-life the concentration of drug in the serum is 50% of the steady-state concentration. After five elimination half-lives the concentration is essentially at its steady-state value. At this point the rate of infusion is equal to the rate of elimination of the drug from the body.

Most drugs are not given as constant intravenous infusions, but as fixed doses at a fixed interval. Figure 2 shows the rise in serum concentration when the same dose per unit time of a drug is given by constant infusion, at intervals equal to the elimination half-life, and at intervals equal to one-half the elimination half-life. The time required to reach steady-state and the mean serum drug concentration are the same for all three schedules; all that varies is the range of fluctuation of serum concentration between doses. The relationships shown in Figure 2 apply to drugs that have rapid absorption and distribution relative to elimination after oral administration.

Table 1 lists the elimination half-lives and time required to reach steady-state serum concentration with chronic oral administration for the five most commonly prescribed antiepileptic drugs. It will be seen that the time required to reach steady-state serum concentration is in fact approximately five times the elimination half-life.

Probably the most important pharmacokinetic relationship to be aware of when administering antiepileptic drugs is that every time a new drug is begun or the dosage of a drug is raised or lowered, one must wait five elimination half-lives to know what the new steady-state serum concentration will be and to know the full therapeutic effect of the medication change. Too often an antiepileptic drug is discarded as ineffective when not enough time has been allowed for attainment of a steady-state concentration. Similarly, the dosage of a drug is sometimes increased too rapidly because not enough time is allowed for reaching steady-state before raising the dose of the drug again. This may result in accumulation of toxic concentrations of the drug.

Another frequent error is to make two changes at the same time in the dosage or type of antiepileptic drug being given. This results in a very complex situation because: (1) different antiepileptic drugs work by different mechanisms; (2) different antiepileptic drugs often have similar side effects; (3) the concentration of the two drugs is changing at the same time, but at different rates; (4) addition or subtraction of drugs may alter the metabolism of other drugs whose dosage is not changed. If good seizure control, increased seizure frequency, drug toxicity, or a large change in the serum concentration of a drug whose dosage was not altered occurs after two or more changes in drug regimen are made simultaneously, the cause of the observed effect is unknown. In non-emergency situations, it is usually best to make only one change in an antiepileptic drug regimen at a time.

Loading Dose. The one compartment, first-order kinetics model predicts that if unit doses of a drug are given intravenously as intervals equal to its elimination half-life, the initial serum concentration after the initial intravenous dose will be one-half the

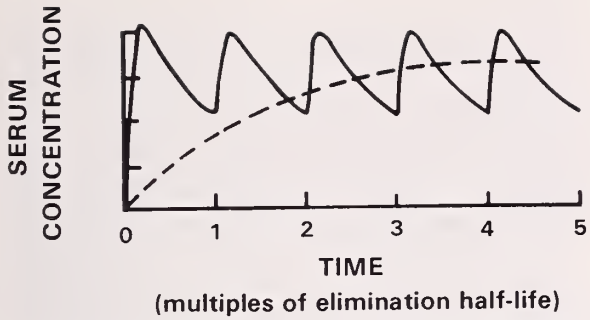

Fig. 3. Predicted kinetic pattern during repeated administration of unit doses of a drug at intervals equal to its elimination half-life after initial loading dose equal to two unit doses. Dashed line shows predicted kinetic pattern for continuous intravenous infusion of drug at a rate of one unit dose per elimination half-life. Modified from Greenblatt and Koch-Weser[22] with permission of the publisher.

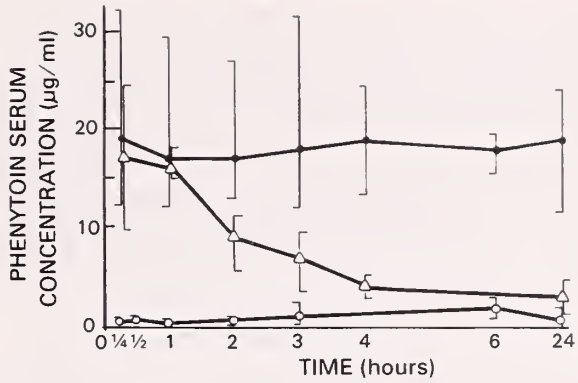

Fig. 4. Range and mean of phenytoin serum concentrations over twenty-four hours with parenteral phenytoin. Dark dots: Twenty-six patients treated with 1000 mg intravenously, 500 mg intramuscularly, and 300 to 500 mg intravenously or orally daily as maintenance doses. Triangles: Five volunteers treated with 500 mg intramuscularly, 500 mg intravenously, and 100 mg intravenously every 6 hours as maintenance doses. Open circles: Six volunteers treated with 500 mg intramuscularly. From Wallis, et al[4] with permission of the publisher.

peak value reached during chronic administration (Figure 2). Figure 3 shows that under these conditions one can achieve steady-state serum concentration immediately if the initial dose is twice the maintenance dose per elimination half-life. This is the principle of the "loading dose," and it is necessary to give such a dose if immediate attainment of therapeutic serum concentration is desired. Figure 4 illustrates that the intravenous administration of 500 mg of phenytoin (a little more than the usual maintenance dose of 300 to 400 mg per half-life of about 24 hours) fails to produce consistently therapeutic serum concentrations (10 to 20 μg/ml), while administration of 1000 mg does. Figure 4 also demonstrates that intramuscular phenytoin is absorbed very slowly. In adults it is necessary to administer a loading dose of 13 to 14 mg/kg of phenytoin to consistently achieve therapeutic serum concentrations.[4,26] In infants the proper loading dose of phenytoin is probably the same or slightly greater.[105] The loading dose of intravenous phenobarbital necessary to consistently achieve therapeutic serum concentrations has not been extensively studied but is probably 8 to 20 mg/kg.[106]

Dosage interval. Pharmacokinetic principles can also assist in choosing a dosage interval for an antiepileptic drug. Ideally, such a drug should be administerd using as long an interval between doses as is practical, because drug regimens requiring frequent administration have poor compliance by outpatients.[107-109] The one compartment, first-order kinetics model predicts that peak serum concentration will increase proportionally with increasing dosage while the duration of serum drug concentration at or above a given minimal therapeutic concentration increases by one elimination half-life with each doubling of dose.[95] Increasing dosage two-fold will increase the peak serum concentration two-fold and will increase the duration of minimal therapeutic serum concentration by one elimination half-life. Increasing dosage by four-fold will increase the peak serum concentration four-fold but will increase the duration of minimal therapeutic serum concentration by only two elimination half-lives. Increasing dosage eight-fold will increase the peak serum concentration eight-fold but will increase the duration of minimal therapeutic serum concentration by only three elimination half-lives. Because of toxicity associated with high peak serum concentrations of antiepileptic drugs, the choice of dosage interval must represent a compromise which maximizes duration of effective serum concentration and minimizes toxicity associated with peak serum concentrations. In practice, antiepileptic drugs whose elimination half-life is 24 hours or longer usually need to be given only once daily to maintain a therapeutic serum concentration.[31,38,110-112] Table 3 illustrates an approximately two-fold range in phenytoin serum concentration when the drug is given once every elimination half-life (i.e., once every 24 hours). The daily dose is usually best given at bedtime to avoid the sedation associated with peak levels of antiepileptic drugs.

TABLE 3

PHENYTOIN SERUM CONCENTRATION FLUCTUATION IN SIX PATIENTS RECEIVING ONCE DAILY DOSES[a,b]

Dose (mg/kg)	*Serum Concentration (μg/ml)* *High*	*Low*
8.0	15	8
5.2	37	19
4.8	26	18
7.5	40	27
5.3	16	7
8.2	29	20

a: Serum phenytoin concentrations were determined 0, 2, 4, 6, 8, 10, 12, 14, 16, and 24 hours after oral dose
b: Modified from Wilder et al (111) with permission of the publisher

COMMENT

The pharmacokinetic principles discussed here

are not intended to be a substitute for clinical judgment or measurement of the serum concentration of antiepileptic drugs. They are intended to help decide when to change the dosage or type of drug being administered, and to help in the interpretation of measured serum concentrations of antiepileptic drugs. The pharmacokinetic principles described above are based on simple models which make many assumptions and have important limitations.[22,23,95,113]

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President's Address*

DOUGLAS R. HILL, M.D.

The poet Goethe once wrote. . . .

"Whatever you can do, or dream you can, begin it. Boldness has genius, power and magic in it."

And so may I begin tonight by expressing my pleasure at having as our honored guests at the head table representatives of our allied professions, and may I extend to each of you fellow physicians and wives and husbands, my thanks for your attendance and participation in this 125th annual meeting of the M.M.A.

During the course of this past year, it was my privilege to attend many functions on your behalf, and at one I heard this story, which I would like to retell, since it contains some profound truths of which we should all be aware.

"Once upon a time there was a sparrow who lived in Presque Isle, Maine. He was brown, chirped happily, worked hard, and had lots of friends. As fall came all his buddies started south, but our hero remained since he was having such a good time. The winds blew colder and colder, and soon he realized he had made a terrible mistake, so he hastily packed his bags and headed south. Cold, fatigue, and exhaustion overcame him however, and he fell to earth in a cow pasture in York, Maine; where he lay quite still, done in. A big friendly cow happened by, and quite by accident, answering the call of nature, covered our hero with a large load of manure. As bad as that was, it had its good side. The manure was hot, and soon the sparrow left *warm* and *comfortable*. Revived with lifted spirits, he ventured a call for help, and his plea was answered by a friendly barnyard cat, who came to his rescue, plucked him from the dung heap, cleaned him off, and proceeded to eat him.

There are three morals to this story:

1. Not all who dump on you are enemies,
2. Not all who come to your rescue are friends,
3. If you are warm and comfortable, keep quiet.

Let's look at these lessons closer:

1. *Not all who dump on you are enemies.*

How often do we complain about being called on to work on committees, collect for the United Way, pay dues to County, State and National Societies, go to Augusta for legislative hearings — so many extra jobs that are put on our shoulders that we have little time for ourselves. All this extra work doesn't come from our enemies, but our friends. They need us just as we need them and we have to respond and carry our fair share of the load.

2. *Not all who come to your rescue are your friends.*

We began with support of Blue Shield, continued with our alliance with Medicare and our compliance with Medicaid. These were to rescue us from the needy patient. But these good friends seem to be taking us toward a medical system completely controlled by our leaders in Washington. With friends like this, who needs enemies.

3. *If you are warm and comfortable, keep quiet.*

That has always been the easy way to deal with the problems of the day, but no one . . . *no one* is going to let us be warm and comfortable any more, *so it won't do us any good to keep quiet.*

What are some of the things that are happening on the National level that will affect the practice of medicine:

1. Health care costs have escalated over the past decade from 1966 to 1976 will annual expenditures climbing from 42 billion to 137 billion. This has spurred proposals such as the Kennedy/Corman Bill. A totally tax financed plan for National Health Insurance, a consumer choice health plan and others in competition with the AMA's Comprehensive Health Insurance Act. Many of the political plans would severely threaten the medical system as we understand it today.
2. The Federal Trade Commission is attacking the AMA for violation of the Sherman Antitrust Act in the areas of price fixing and forbidding of advertising to forestall price competition. They have had us in court two years now, using the tax money of 200 million Americans; ours included, against 300 thousand dues paying members of organized medicine, and it looks like it will be at least another year before it is concluded. They seem to intend to use up our ammunition, money, and wear us down.
3. The Justice Department is waiting in the wings prepared to convene a grand jury if there is evidence.
4. Secretary Califano of HEW remains determined to publish his lists in spite of vigorous AMA and State medical opposition.
5. The Federal Government strains at the leash to place regulatory lids on Hospital costs.

Why do we find ourselves under such bureaucratic attack . . . as one analyst looks at it. . . .

Where the public seems helpless before anticompetitive practices, the bureaucrats are only too willing to step in . . . As witnessed by the last 100 years of American history and a whole series of Government Bureaus; starting with the Interstate Com-

*Presented at the 1978 Annual Session of the M.M.A. House of Delegates.

merce Commission and running through the Securities and Exchange Commission and the Environmental Protection Agency. The pattern is almost always the same. The agency begins by ending the most outrageous practices, then starts looking around for ways to justify its continued existence and expansion. The result is frequently a burden to the taxpayer and endless red tape to the industry or profession involved. On its present course, medicine is heading straight down this path. Health, Education and Welfare has already established the principle of bureaucratic involvement in doctor's affairs through administration of the PSRO (Professional Standards Review Organization) and hospital utilization review committees that monitor Medicare costs and quality. HEW has introduced a measure of consumerism into the conduct of hospital business through the locally selected health systems agencies which have a strong voice in determining how federal dollars are spent on hospitals and facilities. HEW hopes to put new life into the concept of HMO's, and old idea for cost control . . . Full health care for a set price. Doctors work on salary, sharing budget savings or overruns.

Here in Maine we were jolted out of our warm and comfortable seats, when the insurance companies began to withdraw from the malpractice field. Premiums were rising, the JUA was thrown into the gap, the Maine Health Security Act was formulated and the House of Delegates of the M.M.A. just one year ago asked that a search for alternative solutions to the malpractice problem be sought.

A committee chaired by Pat Dowling, supported by Dick Leck, Bill Maxwell and Jerry Morton was formed; and after a year of intense work, the "Medical Mutual Insurance Company of Maine" is a reality and able to issue policies. This truly is a superb example of what can be accomplished. Now it is up to each of us to support this bold venture to assure its success. Ah, but, unless we get too inflated with success, let's look at some other things that happened. . . .

Often we are our own worst enemies. What we say turns out wrong, and what we do backfires. Look for a moment at what happened when we protested the legislatures 10% cut in Medicaid fees as being entirely unilateral. How did it appear in the press? Money hungry doctors angry over fee cuts. We went on to bring suit against Commissioner Smith of the Department of Human Services, and through negotiation had him agree to:

1. Drop the 10% cut,
2. Speed up Medicaid payments,
3. Negotiate an improved fee schedule,
4. Work to have the Certificate of Need requirement for physicians offices dropped.

What actually happened? Very little as yet.

1. The 10% cut was dropped; but, there was no money in the budget to correct the payments.
2. Payments are still months in arrears, although relief is promised by fall.
3. We find that we are currently unable to negotiate with the State with regard to fee schedules.
4. The Certificate of Need provision was dropped; but, according to Dr. John Dow, Chairman of our Committee on Legislation, for all the wrong reasons.

The furor over malpractice and Medicaid subsided, to be replaced by the current hot item, "*The Rising Cost of Medical Care.*" Physicians and hospitals alike are held responsible, and the bureaucracy is leveling an arsenal of weaponry at us to blow us down.

What are some of the practices that the public sees that annoy them with regard to physicians.

1. Expensive diagnostic procedures. Critics say that what the doctor orders seems to benefit him financially, almost as much as it benefits the patient medically; and that it frequently is done solely for the purpose of protecting him against a malpractice suit.
2. Doctors take advantage of economics of scale when they have patients in the hospital. Quick trips, stopping only long enough to ask how the patient is; leaving before there is time to hear the answer, and still getting more than on an office visit.
3. Competition among doctors. Staffs of different hospitals insist on having the latest equipment, i.e., the Cat Scanner.
4. The hallowed tradition of the referral, which the public often views as a "backscratching," even though no fees are split.
5. The 2.4 million unnecessary surgeries performed each year at a cost of 4 billion said to be due to the excess of surgeons.

Not all doctors are guilty . . . But, not knowing where else to turn for redress, the public begins to listen to the politician who promises "to set things right through rules and regulations."

And yet, do we as physicians see these practices as being inflationary to the cost of medical care. I think not. Rather, it seems to me that the single most inflationary pressure I feel is the rising cost of bureaucracy, as expressed by the income tax. This totally unrealistic weapon has never been adjusted for inflation or cost of living increases; and yet, it lies on us as a never ending burden. Governor Longley, in an article from Augusta appearing in a Portland paper said, "In order to control taxes we must control the bureaucracy, which is the greatest single factor in the cancer of inflation which is a malignancy that is tearing away at the hearts and emotions and minds as well as the paychecks of the working men and women and the retired citizens of America." We have an opportunity to express our opinions by our choice and support of candidates in the current Primary Elections, and in the coming elections in the fall.

In what other areas has your medical society been involved. . . .

1. During this year we have tried to improve our inner communications. Often it was felt that the M.M.A., the Pine Tree Organization for PSRO, the Health Care Financing Committee, the M.M.A. Committee for Peer Review and the Legislative Committee were working independently or without adequate understanding of each others goals and objectives. Without some unity of purpose each could flail away like a loose sail. By getting Dave Phillips, a member of the Executive Committee on the PTO, by having Harry Bliss, Chairman of the Health Care Finance Committee attend the Executive Committee meetings, we have brought more unity to our efforts. Major improvements remain to be made in this direction.
2. The impetus of CME has been upheld by the AMA, and our State program under the chairmanship of Jeff Wheelwright has been active in developing CME services. They are planning to broaden their function by. . . .
   A. Developing a CME registry and newsletter.
   B. Developing CME courses for remotely situated hospitals,
   C. Implementation of liaison with the Board of Registration, tying relicensure to CME, perhaps by 1982.
3. In an experimental move last June, the M.M.A. hired a public relations consultant, Mr. James McLoughlin, who has worked throughout the year to better our public image and acceptance. His input and expertise at getting proper coverage and editorial support has been impressive. We have recently video taped six thirty second public service announcements for the M.M.A. beamed to the general public regarding ways to improve their personal health care. His potential has only been partially taped, and should be more fully utilized as our experience and confidence grows.
4. Maine now has a fully funded Health Systems Agency. The HSA established by PL93-641, published guidelines that were truly frightening — Five year plans and inflexible standards that totally superseded community needs and practicalities. HSA found that they have had to back up from their original stand. A recent mailing from HSA has asked all of us to join local community committees of our choice. I hope that you will consider the contribution you might make to one of these committees with regard to the local needs of your community.

The winds of change blow briskly on us all, and if the bureaucrats aren't bringing about enough, then think about the other changes that we face.

We are looking over a precipice within the M.M.A., and it behooves us to say and do the right thing as we enter a period of tumultuous change. The Executive Committee was directed by the House of Delegates to move the office of the M.M.A. to Augusta by 1980. John Wickenden chaired a committee to select a site. Looking ahead, there are architectural and building demands, financing and furnishing problems, all involving organizational and integrated efforts that require the most delicate nuances; and yet, at the same time, the heart of our organization, our leader and Director for over twenty years has expressed his desire to retire. Dan Hanley has been *the* M.M.A. With his twinkling eyes, masterful knowledge, and calm persuasiveness, he has guided us through storm and peril. The Association must move boldly if it is to weather this double jeopardy.

I realize that I have only touched lightly on some of the problems we face . . . what can we do . . . we must begin to act now even while busily engaged in hurried and demanding practices, at the very time when we should be engaged in the painful act of self-examination. It is our tendency to fall back on smug defensiveness rather than to try to defuse the political and bureaucratic threat through change, innovation and reforms of our own initiative.

What can we do personally . . . Well each of us has been called Doc on occasion, probably because someone didn't recall our name, but nevertheless it is a word that we know. Let's take each of those letters and let them stand for something that we can do starting now.

D . . . be doers, . . . get others to be doers. Be active in County, State and National affairs. Go to meetings, support your societies, talk to your legislators, learn the facts, give opinions, lend a hand, stick together, for surely if we don't hang together, they will hang us one at a time.

O . . . be openminded, be ready to change . . . Look at new solutions to old problems, accept new approaches, don't get mired in the mud of the way we used to do it, don't be warm and comfortable.

C . . . care . . . Care personally for each of the patients that you see, care about the quality of care that you render for remember that ultimately, our biggest strength lies in the hands of the people that we care for.

The poet Goethe said, "Whatever you can do, or dream you can, begin it. Boldness has genius, power, and magic in it."

Let us all begin this new year in the M.M.A. with Boldness.

Maine Medical Association

STANDING COMMITTEES — 1978-1979

Standing Committees for 1978-1979 as proposed by the Committee on Nominations and approved at the Second Meeting of the House of Delegates of the Maine Medical Association at Rockport, Maine, June 11, 1978.

Council on Health Manpower and Education

Committee on Allied Health Professions

A. Dewey Richards, M.D., 180 Main St., Orono 04473 (1 yr.) — Chairman
Russell A. Morissette, M.D., 185 Webster St., Lewiston 04240 (1 yr.)
Doris S. Pennoyer, M.D., 112 Vaughan St., Portland 04102 (1 yr.)
Robert G. MacBride, M.D., 25 Washington St., Lubec 04652 (2 yrs.)
Buell A. Miller, M.D., 260 Western Ave., So. Portland 04106 (2 yrs.)
George L. Pauk, M.D., 77 Prospect St., Portland 04103 (3 yrs.)

Committee on Continuing Education

Henry J. Wheelwright, M.D., Augusta Gen. Hosp., Augusta 04330 (1 yr.) — Chairman
Floyd B. Goffin, M.D., Pennellville Rd., Brunswick 04011 (1 yr.)
David H. Skinner, M.D., 169 Academy St., Presque Isle 04769 (1 yr.)
Albert Aranson, M.D., Maine Med. Ctr., Portland 04102 (2 yrs.)
Robert H. Brown, M.D., MRC, Box 45, Bangor 04401 (2 yrs.)
David R. Ginder, M.D., Mid-Maine Med. Ctr., Waterville 04901 (2 yrs.)
Robert L. Ohler, M.D., Box 58, Winthrop 04364 (2 yrs.)
George E. Sullivan, M.D., 100 College Ave., Waterville 04901 (2 yrs.)
Joe R. Wise, Jr., M.D., 263 State St., Bangor 04401 (2 yrs.)
Michael C. Bach, M.D., 97 Campus Ave., Lewiston 04240 (3 yrs.)
William P. Bristol, M.D., 295 Water St., Augusta 04330 (3 yrs.)
Alfred Hurwitz, M.D., 26 Wood Pond Lane, Kennebunk 04043 (3 yrs.)

Committee on Recruitment, Aid & Placement

Ferris S. Ray, M.D., 7 Bramhall St., Portland 04102 (2 yrs.) — Chairman
Charles H. Lightbody, M.D., No. Main St., Guilford 04443 (1 yr.)
A. Dewey Richards, M.D., 180 Main St., Orono 04473 (1 yr.)
Margaret H. Hannigan, M.D., 10 High St., Lewiston 04240 (2 yrs.)
Robert E. McAfee, M.D., 7 Bramhall St., Portland 04102 (3 yrs.)
Donald M. Robertson, M.D., Box 188, Milbridge 04658 (3 yrs.)

Committee on Scientific Programs

David G. Reed, M.D., 108 Elm St., Camden 04843 (2 yrs.) — Chairman
George E. Davis, M.D., 12 Spruce St., Augusta 04330 (1 yr.)
Don L. Maunz, M.D., 186 State St., Bangor 04401 (1 yr.)
Dana M. Whitten, M.D., Medical Bldg., Northport Ave., Belfast 04915 (2 yrs.)
Candace C. Walworth, M.D., 97 Campus Ave., Lewiston 04240 (3 yrs.)
William P. Bristol, M.D., 295 Water St., Augusta 04330 (3 yrs.)
David D. Smith, M.D., Central Maine Med., Ctr., Lewiston 04240 (3 yrs.)

Council on Medical Services

Committee on Care of the Disadvantaged

David C. Dixon, M.D., Box 792, Farmington 04938 (1 yr.) — Chairman
Dorothy I. Eisengart, M.D., 325 Kennedy Mem. Dr., Waterville 04901 (1 yr.)
Stephen A. Sokol, M.D., 10 High St., Lewiston 04240 (1 yr.)
Ruth E. Endicott, M.D., Grasshopper Lane, Ogunquit 03907 (2 yrs.)
John J. Pearson, M.D., 271 Center St., Old Town 04468 (3 yrs.)

Committee on Emergency Medical Services

John W. Towne, M.D., 325C Kennedy Mem. Dr., Waterville 04901 (3 yrs.) — Chairman
Winford C. Adams, M.D., Box 128, Hancock 04640 (1 yr.)
Henry B. Finks, M.D., 22 Lunt Rd., Falmouth 04105 (1 yr.)
Thomas V. Brennan, M.D., 106 Hardy St., Presque Isle 04769 (1 yr.)
Euclid M. Hanbury, Jr., M.D., Medical Bldg., Belfast 04915 (2 yrs.)
Gordon T. Paine, Jr., M.D., Pen Bay Phy. Bldg., Glen Cove, Rockland 04841 (2 yrs.)
John F. Egan, M.D., RFD #3, Box 37A, Turner Rd., Auburn 04210 (2 yrs.)
Frank H. Lawrence, M.D., 22 Bramhall St., Portland 04102 (3 yrs.)
H. Alan Hume, M.D., 295 Water St., Augusta 04330 (3 yrs.)
John C. Menges, M.D., Oak Hill Rd., Fayette 04334 (3 yrs.)

Committee on Government Health Activities

Raymond E. Culver, M.D., 325 Kennedy Mem. Dr., Waterville 04901 (2 yrs.) — Chairman
John H. Steeves, M.D., Rt. #3, Skowhegan 04976 (1 yr.)
Richard B. Stephenson, M.D., 169 State St., Portland 04101 (1 yr.)
Frederick C. Holler, M.D., 10 High St., Lewiston 04240 (2 yrs.)

Committee on Health Care Financing

Harry A. Bliss, M.D., 128 Chadwick St., Portland 04102 (1 yr.) — Chairman
Joseph B. Alley, M.D., 59 W. Main St., Dover-Foxcroft 04426 (1 yr.) — (Piscataquis)
Harold E. Knuuti, M.D., Medical Bldg., Belfast 04915 (1 yr.) — (Waldo)
Jeremy A. Morton, M.D., 321 Brackett St., Portland 04102 (1 yr.) — (Cumberland)
Louis Bachrach, M.D., 85 Baribeau Dr., Brunswick 04011 (1 yr.) — (Linc.-Sag.)
Jerome Dunst, M.D., Rumford Com. Hosp., Rumford 04276 (2 yrs.) — (Oxford)

H. Clement Jurgeleit, M.D., 316 State St., Bangor 04401 (2 yrs.) — (Penobscot)
John Kazutow, M.D., Box 113, Columbia Falls 04623 (2 yrs.) — (Washington)
Harland G. Turner, M.D., Box 38, Norridgewock 04957 (2 yrs.) — (Somerset)
Daniel K. Onion, M.D., RFD #3, Farmington 04938 (2 yrs.) — (Franklin)
Robert I. Roy, M.D., 325A Kennedy Mem. Dr., Waterville 04901 (3 yrs.) — (Kennebec)
Robert F. Ficker, M.D., Maine St., Kennebunkport 04046 (3 yrs.) — (York)
Charles W. Steele, M.D., 472 Main St., Lewiston 04240 (3 yrs.) — (Androscoggin)
Craig W. Young, M.D., A.R. Gould Mem. Hosp., Presque Isle 04769 (3 yrs.) — (Aroostook)
(3 yrs.) — (Hancock)
Peter R. Shrier, M.D., Route 1, Glen Cove 04846 (3 yrs.) — (Knox)

Members of the Advisory Committee to the Committee on Health Care Financing

Maine Society of Allergy and Clinical Immunology — Thomas F. Conneen, M.D., 131 Chadwick St., Portland 04102
Maine Society of Anesthesiology — George W. Bostwick, M.D., P.O. Box 388, Newcastle 04553
Ear, Nose and Throat Group — Loring W. Pratt, M.D., 325 Kennedy Mem. Dr., Waterville 04901
Maine Chapter, American Academy of Family Physicians — David W. Schall, M.D., 56 Baribeau Dr., Brunswick 04011
Maine Society of Internal Medicine (includes Medical Specialty Group) — George E. Davis, Jr., M.D., 12 Spruce St., Augusta 04330
Maine Neurological Society — Edward David, M.D., 498 Essex St., Bangor 04401
Maine Neurosurgical Society — Daniel A. Rock, M.D., 477 Main St., Lewiston 04240
Maine Society of Obstetrics and Gynecology — Buell A. Miller, M.D., 260 Western Ave., So. Portland 04106
Section on Ophthalmology of the M.M.A. — Kevin Hill, M.D, 325A Kennedy Mem. Dr., Waterville 04901
Maine Academy of Orthopedic Surgeons — Robert B. Day, M.D., 75 Stone St., Augusta 04330
Maine Society of Pathologists — Richard C. Leck, M.D., Bath Mem. Hosp., Bath 04530
Maine Chapter, American Academy of Pediatrics — Charles E. Burden, M.D., 1 North St., Bath 04530
Maine Psychiatric Association — Aldo F. Llorente, M.D., Moulton Union, Bowdoin College, Brunswick 04011
Maine Radiological Society — John F. Gibbons, M.D., 22 Bramhall St., Portland 04102
Maine Chapter, American College of Surgeons — John F. Reynolds, M.D., 325 Kennedy Mem. Dr., Waterville 04901
Maine Urological Society — Bruce D. Nelson, M.D., 103 State St., Portland 04102

Committee on Hospital Association Liaison

Euclid M. Hanbury, Jr., M.D., Medical Bldg., Belfast 04915 (2 yrs.) — Chairman
Paul J. Killoran, M.D., Pen. Bay Med. Ctr., Glen Cove, Rockland 04841 (1 yr.)
Richard C. Leck, M.D., Bath Mem. Hosp., Bath 04530 (2 yrs.)
John F. Gibbons, M.D., 22 Bramhall St., Portland 04102 (3 yrs.)

Committee on Peer Review

George W. Wood, III, M.D., 840 Broadway, Bangor 04401 (2 yrs.) — Chairman
Robert F. Ficker, M.D., Maine St., Kennebunkport 04046 (1 yr.)
Hans A. Holzwarth, M.D., 336 Mt. Hope Ave., Bangor 04401 (1 yr.)
Richard M. Swengel, M.D., 477 Main St., Lewiston 04240 (1 yr.)
William O. Buell, M.D., 22 Jefferson St., Box 736, Biddeford 04005 (1 yr.)
Elihu York, M.D., 82 Baribeau Dr., Brunswick 04011 (1 yr.)
T. Craig Childs, M.D., P.O. Box 285, Belfast 04915 (2 yrs.)
David G. Reed, M.D., 108 Elm St., Camden 04843 (2 yrs.)
John Kazutow, M.D., Box 113, Columbia Falls 04623 (3 yrs.)
Peter Leadley, M.D., Box 706, Augusta 04330 (3 yrs.)

Council on Medicine and Law

Committee on Ethics, Discipline and Professional Competence

John E. Knowles, M.D., 52 Gilman St., Portland 04102 (1 yr.) — Chairman
Peter F. McGuire, M.D., 56 Baribeau Dr., Brunswick 04011 (1 yr.)
Linus J. Stitham, M.D., 50 Main St., Dover-Foxcroft 04426 (1 yr.)
Waldo A. Clapp, M.D., 215 College St., Lewiston 04240 (2 yrs.)
Robert H. Dixon, M.D., 20 York St., Bath 04530 (2 yrs.)
Thomas W. Williams, M.D., Pen. Bay Phy. Bldg., Glen Cove, Rockland 04841 (3 yrs.)

Committee on Legislation

John P. Dow, M.D., Grove Hill, Pittsfield 04967 (1 yr.) — Chairman
Brinton T. Darlington, M.D., 32 Westwood Rd., Augusta 04330 (1 yr.)
Francis I. Kittredge, M.D., 498 Essex St., Bangor 04401 (1 yr.)
Euclid M. Hanbury, Jr., M.D., Medical Bldg., Belfast 04915 (1 yr.)
Kevin Hill, M.D., 325A Kennedy Mem. Dr., Waterville 04901 (2 yrs.)
John H. Shaw, M.D., Pond Rd., Manchester 04351 (2 yrs.)
Martyn A. Vickers, Jr., M.D., 14 Glenridge Dr., Augusta 04330 (2 yrs.)
Ulrich B. Jacobsohn, M.D., 130 Main Ave., Farmingdale 04345 (2 yrs.)
Carl E. Richards, M.D., Box B, Alfred 04002 (3 yrs.)
James H. Bonney, M.D., 53 Chadwick St., Portland 04102 (3 yrs.)

Committee on Professional Liability

Thomas A. Martin, Sr., M.D., 157 Pine St., Portland 04102 — Chairman
James H. Bonney, M.D., 53 Chadwick St., Portland 04102
George L. Maltby, M.D., 31 Bramhall St., Portland 04102
John A. Root, M.D., Pen. Bay Phy. Bldg., Glen Cove, Rockland 04841
Allan J. Stinchfield, M.D., 16 E. Chestnut St., Augusta 04330

County Society Notes

Penobscot

The April meeting of the Penobscot County Medical Society was held on April 18, 1978 at the Killarney Restaurant in Bangor. About 50 members and guests attended.

The meeting was opened by the President, Dr. Philip G. Hunter; the minutes of the March meeting were approved. The April Newsletter covered most of the significant activities at the State and local level and, thus, these were not reiterated. A recent communication from Blue Cross and Blue Shield announced voluntary coverage for a second surgical opinion; this was the preview of a proposed press release to be distributed within several weeks; the plan is to be effective in Fall of 1978. Dr. Hunter then read a letter from Dr. Leonidas regarding the unintelligible language of many insurance policies. A motion was made by Dr. Holzwarth that Dr. Lightbody, a member of the Board of Directors of Maine Blue Cross and Blue Shield, bring this matter up to that organization at their forthcoming annual meeting on April 19, 1978.

Drs. David Dixon and Daniel Onion, of the Rural Health Associates from Farmington, then presented a very enlightening discussion of their organization — its development, growth, some of their problems and also some of the major attributes of the system. A lengthy question and answer period followed.

The meeting was adjourned at 10:00 p.m.

H. Clement Jurgeleit, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association met in a joint meeting with the Kennebec County Bar Association on April 20, 1978 at John Martin's Manor Restaurant in Waterville.

The minutes of the previous meeting were approved. The applications of Drs. Alexander Wall, Herbert Bartholomew and Clifford Nemeth were favorably acted upon. The application of Dr. H. B. Richardson was read. There being no further business, the floor was opened for a joint discussion between the members of the Medical Association and the Bar. There was no particular area of business to be discussed. The members of the two organizations discussed mutual problems about professional relationships and the nature of the two professions for some 30-45 minutes and the meeting was adjourned.

O. Thomas Feagin, M.D., *Secretary*

Franklin

The Franklin County Medical Society met on June 5, 1978.

The meeting was chaired by the President, Dr. James R. MacMahon.

Dr. Burgess Record presented a description of an upcoming study on hypertension using acebutolol and acebutolol plus thiazide in a blinded fashion. After describing the study, he asked for and received voted approval by that County Medical Society of this study. In addition, he encouraged members of the County Society to send patients who are difficult to control or who could benefit from a year's worth of free hypertension evaluation and medication to the study.

Dr. Daniel K. Onion and Dr. Gaetano Fiorica went through the twelve resolutions that will be presented to the House of Delegates at the Maine Medical Association Annual Meeting and received non-binding direction from the County Medical Society about how they should vote on each of these resolutions.

Daniel K. Onion, M.D., *Secretary*

Letters to the Editor

To the Editor:

Valproate

The Food and Drug Administration approved valproate (valproic acid), a prescription drug for the treatment of patients with a certain type of epilepsy.

The drug was approved for the treatment of patients who suffer temporary seizures in which they lose consciousness for a few seconds, a condition known as petit mal epilepsy.

Valproate is likely to be useful in the treatment of a significant number of epileptic patients who do not respond well to currently-available drugs.

The drug will be sold in capsule and liquid form by Abbott Laboratories under the brand name Depakene.

Dr. Julius Richmond, Assistant HEW Secretary for Health and a pediatrician, welcomed the approval decision. "Children and young adults with epilepsy especially stand to benefit because the kind of seizures for which valproate is most effective often interrupts the learning process or makes it impossible," he said.

The type of seizures most responsive to valproate frequently affects the young, but also occur in epileptics of all ages.

Dr. Richmond called the valproate decision "an excellent example of the FDA scientific regulatory process working efficiently and objectively in the face of strong emotions and partisan pressures."

Abbott applied for FDA approval on September 22, 1977. On December 14, 1977, FDA identified additional medical data needed to demonstrate the safety and effectiveness of the drug. Abbott submitted these data on January 30, 1978.

While FDA was reviewing the company's application, the drug was made available with FDA's permission to more than 1,000 patients with special needs for it.

The prescribing information for physicians approved by FDA says the most common side effects when first taking the drug are nausea, vomiting and indigestion. These effects are usually transient.

The labeling says liver failure resulting in death has occurred in a few patients taking the drug along with other antiepileptic drugs, and that physicians should perform liver tests before prescribing valproate and periodically thereafter.

The drug also may depress the central nervous system, and patients should not drive or operate dangerous machinery until it is clear how they react to it.

In addition, valproate increases the depressant effects of alcohol, and physicians should exercise caution in prescribing it with certain other drugs, especially barbiturates.

HEW News
U.S. Department of Health, Education, and Welfare

To the Editor:

The Independent Order of Foresters is the largest nonsectarian family fraternal benefit society in the World. One of the early strongholds where the Foresters flourished was in the great State of Maine; at one time there were over One Hundred and Twenty-Five local courts (lodges) here.

As we are starting to rebuild the membership of the Foresters in Maine, we wondered if any of your readers had in their possession any memorabilia relating to the Independent Order of Foresters, (regalia, certificates, banners, charters, collars, badges, documents, insignias, etc.), they may care to inform us about them or let us have.

Any help that we can get will be greatly appreciated, thank you.

Eric Davies
State Organizer
The Independent Order of Foresters
250 Route #1
Scarborough, Maine 04074

Librax®
Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br.

Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCl and/or clidinium Br.
Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants, and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Physical and psychological dependence rarely reported on recommended doses, but use caution in administering Librium® (chlordiazepoxide HCl) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) reported following discontinuation of the drug.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy. Advise patients to discuss therapy if they intend to or do become pregnant.**

As with all anticholinergics, inhibition of lactation may occur.
Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established.
Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated; avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, *i.e.*, dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

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Letters to the Editor

To the Editor:

Your cooperation is requested in the referral of patients with pediatric malignancies for studies being conducted by the Pediatric Oncology Branch, National Cancer Institute, at the Clinical Center, National Institutes of Health, Bethesda, Maryland.

Patients with acute leukemia, neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma, osteogenic sarcoma, and non-Hodgkin's malignant lymphoma (especially Burkitt's lymphoma) are eligible for these studies. Patients selected for the program will generally have received no previous definitive therapy, and will usually be under the age of 30 years. Clinical trials involve evaluation of new combinations of chemotherapy, immunotherapy, radiotherapy, and surgery. All patients accepted for admission to this Branch may also be enrolled in studies of optimal supportive care techniques (e.g., autologous bone marrow infusion, platelet and granulocyte transfusion, and laminar-airflow protective isolation). Patients may be admitted with any stage of their disease, except in the case of neuroblastoma studies which are restricted to Stages III and IV.

The referring physicians will be kept fully informed as to the results of treatment and are encouraged to participate in the follow-up care of their patients. Patients may withdraw from the program upon request by the individual or the referring physician. There will be no cost to the patient for evaluation, treatment, travel (except for the first admission), hospitalization, or ambulatory care related to these clinical trials.

Physicians interested in further details or in having their patients considered for admission may contact: Attending Physician, Pediatric Oncology Branch, National Cancer Institute, Clinical Center, Room 3B-12, National Institutes of Health, Bethesda, Maryland 20014 (301-496-4256).

Thank you for your consideration.

ARTHUR S. LEVINE, M.D.
Chief, Pediatric Oncology Branch
National Cancer Institute

To the Editor:

In your role of caring for patients with arthritis, the Arthritis Foundation is offering you an opportunity to do some clinical research related to arthritis.

In 1956, Mrs. Florence Kerrison left the Foundation and other health organizations some money for research in Maine.

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1979 July 22-26 Chicago
1980 July 20-24 Chicago

INTERIM MEETINGS — HOUSE OF DELEGATES
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1979 December 2-5 Honolulu

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Carcinoma of the Male Breast

JAMES GEORGITIS, M.D.*

Carcinoma of the male breast is uncommon. It is rare for a surgeon to encounter more than a few cases during a lifetime. It constitutes between 0.38% to 1.5% of male cancers and afflicts 600 men in the United States annually.[1] In comparison, breast cancer constitutes 23% of female malignancies. The incidence of carcinoma of the male breast is in accord with the rule that cancer occurs infrequently in vestigial organs.[2] Male breast cancer accounts for .15% to .30% of deaths in males over 25 years in comparison to 18.9% to 36% in females.[1] Statistics regarding female breast cancer are not thought to be comparable to male breast cancer because of the difference in anatomy and frequency with which adjacent structures are involved. Fourteen cases of breast cancer in males presenting at two Portland, Maine hospitals are evaluated and presented.

CASE REPORTS

Materials and Methods

From July 1968 to July 1977, fourteen men with carcinoma of the breast were admitted to the Mercy Hospital or Maine Medical Center in Portland, Maine. Historical information provided in the records was reviewed for previous malignancy, mode of discovery, past history of gynecomastia, and specific medication use (hormone, diuretic, or digitalis). Duration of symptoms and length of time until surgical intervention were evaluated. Physical findings, location, size of mass, presence or absence of skin retraction, chest wall fixation, axillary node involvement, nipple ulceration, nipple discharge or crusting were tabulated. Pathological diagnosis and therapeutic modes utilized were correlated with staging and survival.

Results

All fourteen patients were Caucasians. Ages ranged from 38 to 91 with a mean of 68.2 years. All but one patient had surgical therapy. A patient of 91 years was considered to be an unreasonable anesthetic risk and needle biopsy for diagnosis was undertaken only.

Two patients had a previously treated breast cancer of the opposite breast (treated 7 and 10 years previously). Three additional patients had other malignancies (osteogenic sarcoma, parotid tumor, melanoma) treated prior to the appearance of breast cancer. Two patients had a family history of breast cancer in female siblings and one patient had a brother with breast cancer. Thus, a total of 6 of 14 (42%) patients had a previous history or a family history of malignancy.

Self examination led to the identification of a "lump" in 8 of 14 patients (57%). A physician identified a mass in the remaining 6 patients. Gynecomastia was noted in past physical examinations in five instances (35%). Only one patient had received hormonal therapy and this was thyroid replacement. Three patients used diuretics and two, digoxin for symptomatic congestive heart failure.

The most frequent sign was a breast mass or nodule in 6 of 14 patients. Ulceration of the nipple in three patients and painless bleeding from the nipple in two others led to surgical consultation. Pain was present in three cases. Duration of localized breast pain from four to twelve months was noted in these patients. The average delay from onset of symptoms until seeking medical attention was 2.7 months, with a range of one week to two years.

The clinical findings of carcinoma of the male breast are more uniform than in females for obvious reasons. The tumor size is more accurately assessed on palpation and fixation easily determined. Involvement of the left breast was noted in 8 of 14 patients (57%) and of the right breast in six. Masses ranged from 1 to 3 cm., the average size being 1.8 cm. Skin retraction was noted in 8 patients, ulceration in 4 patients and a fungating mass in one patient. Nipple retraction was present in 6 of 14 patients (43%), nipple discharge in 2 of 14 patients and nipple crusting was present in one patient. No case of Paget's disease was noted. Metastatic satellite involvement to the chest wall was noted once. Axillary nodal involvement was detected preoperatively in two patients.

Histologic examination in seven instances were described as infiltrating ductal carcinoma, four as scirrhus carcinoma and three as adenocarcinoma. In five of fourteen cases that had modified or radical mastectomy, pathological involvement of axillary nodes was noted.

Preoperative staging is tabulated in Table 1. Surgical therapy was undertaken in 13 instances. Nine patients were treated with modified radical mastectomy, two with simple mastectomy. Two patients had standard radical mastectomy and one patient had only needle biopsy for diagnosis.

Postoperative complications occurred only in those treated with modified radical mastectomy. Three patients had significant postoperative hemorrhage, one on the 8th postoperative day. One patient had a small hematoma aspirated and one the drainage of a seroma. Five patients were subsequently treated with radiotherapy

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Table 1

Primary Treatment of 13 Males With Breast Cancer

Age	Stage	Operation	Axillary Lymph Nodes	Postoperative Treatment	Follow Up Period	Outcome
88	II	Simple Mastectomy	(+)	Radiotherapy & Bone Bx	12	Expired of Metastatic Disease
74	II	Modified Radical Mastectomy	(−)	—	24	F.O.D.
50	I	Simple Mastectomy	(−)	—	24	F.O.D.
51	IV	MRM	(+)	—	96	F.O.D.
70	III	MRM	(+)	—	48	Expired of Metastatic Disease
67	II	MRM	(−)	—	60	F.O.D.
71	II	MRM	(−)	(−)	24	F.O.D.
38	II	Modified Radical Mastectomy	(+)	Radiotherapy & Chemotherapy	12	F.O.D.
82	I	MRM	(+)	Radiotherapy	12	F.O.D.
77	II	MRM	(−)	Radiotherapy	108	Expired of Metastatic Disease
62	II	MRM	(+)	—	12	F.O.D.
64	III	RM	(+)	—	24	F.O.D.
71	III	RM	(+)	Radiotherapy & Orchiectomy	12	F.O.D.

and one patient underwent subsequent orchiectomy.

Recurrence of tumor at the site of excision occurred in three patients, all within a year of initial excision. One patient required excision twice for recurrency but survived 10 years. Three patients expired with metastatic disease with an average survival of 56 months. Eight patients are alive and free of clinical disease for an average of 32.4 disease free months.

Table 2

Clinical Staging of 14 Cases of Male Breast Cancer

TNM Stage	Cases	Percentage of Cases
I	2	14%
II	8	57%
III	3	21%
IV	1	7%

Discussion

The earliest recorded case of breast cancer was in a male, Imhotep, in 3,000 B.C. in case 45 of the Edwin Smith Papyrus, entitled Instructions Concerning Bulging Tumors on His Breast, noted the following:

"If thou examinest a man having bulging tumors on his breast and thou findest that swelling has spread over his breast; if thou puttest thy hand upon his breast upon these tumors and thou findest them very cool, there be no fever at all therein when thy hand touches him; they have no granulations; they do not generate secretions of fluid; and they are bulging to thy hand, the diagnosis thou should say concerning him — one having bulging tumors, an ailment with which I will contend — there is no treatment."[3]

The etiology of male breast cancer remains undefined even at this time. There is no known relationship with previous history of trauma, radiation, gynecomastia or drug exposure.[1] The previously reported high incidence of breast cancer in men treated with estrogen for disseminated prostatic car-

cinoma was, in fact, metastatic involvement of breast tissue.[4] Some correlation has been noted between a prior history of orchitis and breast cancer in comparison to controls.[5] Bilateral testicular atrophy following mumps orchitis with elevated FSH levels has been correlated with breast cancer, as has Klinefelter's syndrome which also has altered estrogen metabolism.[4] However, neither of these accounts for a significant number of cases of male breast cancer.

Male breast cancer has been alleged to have regional incidence. A higher incidence of breast cancer in males is noted in North America than in Finland and in the northeast of the United States in comparison to the rest of the country.[6,4] However, not enough cases have been collected to make any of these statements statistically significant. There is no association of breast cancer with religious preference, geography, race or occupation.[7]

The average age of presentation with breast cancer for males is 60 years.[4] The peak age incidence is 6 to 11 years later than in females and no bimodel curve is noted as it is in females.[4] A predominance of left sided male lesion 1.07 to 1[4] has been noted and was present in this study. No previous reference concerning family history of malignancy in association with male breast cancer is noted in the literature.[4] Our series suggests that a family history of breast cancer and/or the presence of a previous malignancy may be correlated with male breast cancer.

The association of previous malignancy, family history of breast cancer, gynecomastia and estrogen displacing medication (digitalis, diuretics) suggests that a hormonal effect on the presence of an appropriate genetic background may effect malignant changes in a vestigal structure. Estrogen receptor assay may offer insight into this relationship.

Ninety percent of patients in a composite series presented with a subareolar mass that was rarely discovered by self breast exam.[4] The number of patients who discovered a "lump" in this series of patients suggests that more patient awareness is present than was appreciated in the past. Nipple discharges is a more frequent symptom than in female breast cancer. It has been reported to be present in 13.7% of males with breast cancer and in only 2.1% of males with benign breast masses. It is usually a serious discharge when benign, as it is with females. However, bloody discharge was associated with carcinoma in 75% of cases in males, three times its incidence in females. In 12.5% of cases in composite series, bilateral carcinoma is present.[4] This series reflects both of these findings.

Earlier, an average of 18 months delay occurred from the time of onset of symptoms until treatment was initiated.[4] This improved to 10 months in the last two decades[4] and was only 2.7 months in this series. In Scheike's series,[9] 54% were stage III and IV as compared to 28% in this series. This may reflect earlier surgical evaluation in this series of patients.

There is a high incidence of nipple and areolar abnormalities. Ulceration has been present in 28% of patients. Fixation, edema, inversion or encrustation are present in an additional 37%. Our series similarly reflects these findings.

The differential diagnosis is benign gynecomastia versus carcinoma. History of drug use and resulting gynecomastia should be noted but does not exclude carcinoma. Gynecomastia is suggested by bilaterality, youth, pain without ulceration, and previous estrogen therapy. Pectoral fixation and ulceration are rarely present. The benign fibroepithelial hyperplasia of gynecomastia is usually well delineated and discoid, with pubertal tenderness frequently noted.

No correlation between histological grading and prognosis has been noted.[4] There appears to be a difference in Paget's disease in the male breast in that it lacks the invasion of underlying ductal carcinoma in contradistinction to female breast cancer.

The therapy of male breast cancer is still not fully resolved. Few studies have defined criteria for operative selection other than to note an aversion to radical mastectomy because of excessive blood loss and high frequency of skin grafting. This is necessitated by early epidermis, pectoral fascia and axillary node involvement. In 1927, the five-year survival was 19%,[11] in 1940, 47%,[4] in 1960, 41% to 47%,[4] and in a combined series average was 36%. Axillary node involvement is frequent—53%[1] in a series of 191 males.

The poor survival rates of male breast cancer (36% 5-year survival) as compared to that of females (45% 5-year survival in females with ulceration, retraction, for fixation) may reflect early involvement of adjacent tissue which predisposes to internal mammary lymph node and axillary node involvement. In fact, in the female statistics for central breast cancer, 38% 5-year survival compared to 53% for medial and 53% for lateral lesion are strikingly similar to survival statistics for male breast cancer.[4]

Survival statistics for male breast cancer have remained essentially unimproved for the last fifty years. The early involvement of superficial adjacent tissue with metastatic spread to axillary and internal mammary lymph nodes may explain the unimproved statistics. Careful consideration should be given to adjuvant radio-therapy direct at nodal tissue which combined with earlier surgical therapy may improve survival.

Summary

Carcinoma of the male breast is rare, constituting only 1.5% of male cancers. Fourteen cases are evaluated with specific reference to historical information, physical findings and operative therapy. Prognosis appears to be worse than in females and

Continued on Page 260

Curative Radiation Therapy for Early Breast Cancer

HUGH M. PHELPS, M.D.*

Breast cancer is the leading cause of cancer deaths in women in the United States. In spite of its high incidence, the proper treatment of this disease is far from established. The management of breast cancer is controversial because of questions concerning the extent and type of surgery, the need for elective postoperative radiotherapy, and the indications for adjuvant chemotherapy.

Since its introduction, the Halstead radical mastectomy has become the accepted standard of practice, to which all alternative procedures must be compared. In recent years, data has been generated that indicates that radical radiotherapy following lumpectomy or excisional biopsy, provides very comparable local control and survival rates, at the same time resulting in quite acceptable cosmetic results.

This communication is intended to review (1) the principles of treatment of breast cancer, (2) the surgical and radiotherapeutic results in the literature, and (3) current radiation treatment policies.

Principles of Management of Breast Cancer

Radical surgery and radical radiation therapy are loco-regional treatments only. Five-year survival rates have been demonstrated to be unrelated to type of local treatment, whether ultraradical mastectomy (including internal mammary node dissection) or radiation therapy alone.[1] However, adequate local therapy must be administered if a cure of breast cancer is sought. It has been amply demonstrated that distant dissemination of disease is now the major hurdle in achieving this goal. Systemic modalities (chemotherapy) are a rational means of controlling distant disease, and the early results in this regard are encouraging.[2]

Since distant metastatic disease now appears to be the limiting factor in the cure of breast cancer, it is prudent to consider the least morbid and most acceptable form of local therapy, assuming that these differing modalities will result in equivalent local control rates.

There are now several studies of patients treated with curative radiation therapy which support the concept that ionizing radiation can provide local control rates equivalent, and perhaps superior to, conventional radical surgery.

Radiation Therapy as Primary Treatment

As early as the 1940's, patients with breast cancer were treated definitively with ionizing radiation. In North America, the indications for this unorthodox treatment were usually patient refusal of mastectomy or medical contraindications to major surgery. Because of the limitations in equipment and technique, these patients received what presently would be considered suboptimal treatment. Nevertheless, local control and survival rates were similar to mastectomy patients.[3,4,5]

These methods of treatment were not widely used for a variety of reasons, including technical limitations as well as patient and physician resistance. The relatively recent advances in computerized radiotherapy treatment planning, therapy machines (linear accelerators) and the availability of interstitial treatment modalities (afterloading iridium 192) have allowed more reliable sterilization of malignant disease with fewer radiation complications.

A dose response curve has been established for successful radiation treatment of breast cancer.[6] For sterilization, microscopic disease requires 4500-5000 rads in 5 weeks (external beam treatment). Masses 2-3 cm. in diameter require 6000-7000 rads. Larger masses necessitate comparably larger doses. Doses above 5000 rads to localized areas can be delivered using interstitial radioactive sources. On this basis, performance of an excisional biopsy allows lower but adequate doses of radiation to be given to residual microscopic disease.

In a landmark study, Prosnitz, et al,[7] reported results which appear quite favorable with respect to both survival and local control when compared with similarly staged mastectomy patients. A total of 49 patients with clinical Stage I disease (UICC TNM staging criteria) from four institutions (Yale, Harvard, Thomas Jefferson University and Hahnemann Medical College) were treated with radical radiation therapy. Forty-two of the 49 are free of disease between 2 and 13 years following treatment with an actuarial relapse-free survival of 91% at 5 years. Five patients died of intercurrent illness, but free of cancer. There was one local failure (2%).

One hundred and one Stage II patients were similarly treated, with relapse-free actuarial survival of 60% at 5 years. The local recurrence rate was 9%. One-half of the local failures were salvaged by mastectomy.

The five-year survival rates in this study are quite comparable to those obtained by radical mastectomy. The local recurrence rates are substantially less than those reported for mastectomy alone, and ap-

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TABLE 1

STUDY	NUMBER PATIENTS	SURVIVAL	LOCAL RECURRENCE	FOLLOW UP TIME
Prosnitz, L.[7]				
Stage I	49	91%)Actuarial	1/49 (2%)	1-13 years
Stage II	101	60%) at 5 years	9/101 (9%)	
Pierquin, B.[8]				
Stage I & II	225	Unstated	2/225 (0.9%)	Unstated
Cope, O.[9]				
Stage I	22	73%	8/81 (10%)	minimum 5 years
Stage II	43	63%		
Brown, S.[10]				
Stage I & II	100	70% actuarial at 5 years	2/100 (2%)	Average 3.4 years (1-17 years)
Ghossein, N.[11]				
Stage I and II	36	72% 3 years	2/36 (5.5%)	Average 3 years
Representative Surgical Series (from Prosnitz)				
Stage I	1569	75-85%	10-20%	5 years
Stage II	695	50-60%		

proximately equal to radical mastectomy plus post-operative radiotherapy.

Other studies showing similar trends of excellent local control and comparable (although in some cases early) survival figures are shown in Table 1. For comparative purposes, data collected from a number of studies involving surgically treated patients are included.

Present Treatment Policies—Pre-radiation

All patients who are considered candidates for radical radiation therapy would optimally have an excisional biopsy (lumpectomy) of the breast mass, both for diagnostic purposes and for debulking of gross disease. This can be done under either local or general anesthesia, at the surgeon's discretion. If gross disease is resected, subsequent lower radiation doses can be utilized with less likelihood of unacceptable radiation morbidity. Wide surgical margins around the tumor are not advised except with small, easily resected tumors, for better cosmetic results can be obtained by treating the tumor bed with an interstitial implant of iridium 192.

At present, it is advisable to excise a few of the lower axillary lymph nodes for staging purposes. This is usually done through a separate, small low axillary incision. Information obtained here is helpful in making decisions about subsequent chemotherapy, especially in pre-menopausal women.

Radiation Treatment Policies

Following lumpectomy, patients are initially treated by external beam megavoltage equipment (usually a linear accelerator or cobalt unit). Parallel opposed, wedged tangential fields, encompassing all mammary tissue, are used. In addition, axillary, supraclavicular, and internal mammary nodes are treated. Doses of approximately 5000 rads in 5 weeks are delivered. Detailed isodose plots, preferably computer derived, are required to reliably deliver a homogeneous dose to target areas.

In many patients, a localized treatment boost is given with interstitial iridium 192. This isotope lends itself to afterloading with the consequent elimination of radiation exposure to operator and operating room personnel. A simple system utilizing readily available Angiocaths as the carriers for iridium has been developed. The Angiocaths can be inserted under either local or general anesthesia. Computer generated isodose plots are obtained which allow considerable precision in dose determination. Typically, an implant will remain in place for 24-36

hours, delivering 1500-3000 rads.

Complications

Serious long-term complications have been quite infrequent in patients treated in the above manner. The most serious is that of radiation pneumonitis, which occurred in 4 of the 150 patients in the Prosnitz study group.[7] This complication, which is usually self-limited, can be minimized with careful attention to field alignment, and successfully treated with small doses of corticosteroids.

Fibrosis is usually minimal after 5000 rads of external beam treatment to the whole breast. Local induration is occasionally seen following interstitial iridium.

External beam doses above 5000 rads (required for very large tumors) and treatment of large, pendulous breasts can be expected to cause varying degrees of diffuse fibrosis.

The cosmetic results of treating early breast cancer in the non-obese patient have been considered good to excellent.

Summary

1. Radical radiation therapy is an acceptable alternative to radical mastectomy. Local recurrence and survival rates for the two modalities are comparable.
2. Pre-irradiation procedures should include limited excisional biopsy (lumpectomy) and for chemotherapeutic decision-making, low axillary node sampling through a separate incision.

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A Vaginal Approach to Preservation of Ovarian Function in Pelvic Node Radiation

Stanley W. Kent, M.D., Louis G. Bove, M.D. and Hugh M. Phelps, M.D.*

Abstract

A case is presented in which a 14-year-old girl with Hodgkin's disease had ovarian fixation by a wire suture placed via the vagina prior to pelvic node radiation. She subsequently had normal periods and continued to have regular periods five years later.

Attempts to preserve ovarian function during radiation for Hodgkin's lymphoma in the young females have become widespread in recent years. In order to do this, various forms of ovarian fixation prior to radiation have been tried. The first recorded attempt at ovarian fixation was carried out by Kovacev in 1954.[2] He exteriorized the ovaries after a Wertheim operation by taking them out through the flank muscle on each side. These ovaries typically developed cysts "up to the size of an apple" and required repeated transcutaneous aspirations. Another innovative approach was reported by Batten in 1956[1] in which he devised portable lead shells to be sutured over the ovaries and left in place during x-ray therapy. These shells would not be practical with today's high voltage radiotherapy methods. Trueblood, et al, in 1970,[6,7] reported a fairly simple method of fixation of the ovaries to the front and back of the fundus which could be carried out at the time of a staging laparotomy. Although the tubes and ovaries were in a rather unusual position, fertilization has taken place and several successful pregnancies have been described.[3] A modified lateral fixation has been reported by Nahhas, Lewis et al, in 1971,[5] where the ovary was dissected away from its connection to the tube and fixed laterally on the psoas muscle. This appears to leave a wide separation between tube and ovary making subsequent fertilization difficult. One of the authors has stated however that pregnancies have taken place and that the procedure has proven very practical on his service.[4]

The above methods are all applicable only when a laparotomy is contemplated. In instances where no laparotomy is contemplated prior to radiation, a vaginal approach should be considered. The following case report illustrates the method employed.

Case Report

This 14-year-old girl was referred for ovarian fixation in 1972. She had presented to her physician with fever, anemia, and splenomegaly and, after an exhaustive workup, she underwent an exploratory laparotomy for diagnosis. Findings at surgery revealed Hodgkin's disease (mixed celluarity) arising from the splenic pedicle and extending to the tail of the pancreas and greater curvature of the stomach. No other metastatic disease was identified; and a complete staging laparotomy with liver biopsy was done. She was staged Hodgkin's disease, mixed celluarity, IV-B. She then received chemotherapy from January, 1971 to December, 1971. She originally received three courses of MOPP (Nitrogen Mustard, Oncovin® , Procarbozine, and Prednisone) in standard dosage. Because of persistent fever, night sweats, and anemia, this program was switched to Velban® 7.5 mg. I.V. q two weeks and Prednisone daily. Within a month after the institution of therapy with Velban and Prednisone, she was afebrile and symptomatically improved. This program was continued for eight months, making the total period of chemotherapy eleven months.

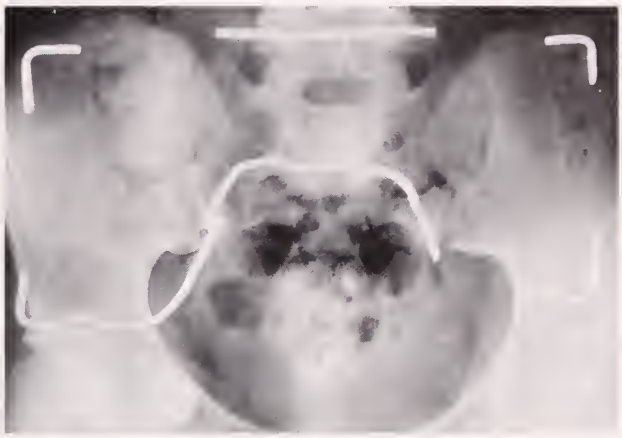

Fig. 1. Portion of abdominal film showing pelvic fields and wire suture in place.

She then received external upper abdominal radiation by strip technique from December 1971 to February 1972. This gave about 2600 rads to most treated areas.

She was admitted to the hospital and had a midline episiotomy, culdotomy, and vaginal suture of the ovaries on 1-11-72. A #2 stainless steel wire was passed up through the cervix, out the back of the uterus through both ovaries and out through the posterior fornix. A lead bead was placed on each end of the suture (Fig. 1). She then had radiation to the pelvis given by a single pair of parallel opposed portals blocking out the ovaries as seen radiographically. She received a total of 2350 rads in nine fractions, giving a biological equivalent of 3200 rads in sixteen treatments. She was then readmitted for removal of the suture. Following this, she resumed normal menses within four months and finished her radiotherapy with a dose of 3000 rads to the upper mantle. She was last seen on 9-26-77 when she complained of severe dysmenorrhea with regular menses. Examination showed no evidence of recurrent lymphoma. The perineum appeared nulliparous. The uterus was anterior and normal size. The right ovary was movable and soft. The left ovary was fixed to the cervix.

The above technique has the advantage of avoiding another laparotomy, moving the ovaries further from the pelvic nodes, and finally leaving the ovaries in functional operation.

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Serum Alpha-1-Antitrypsin Deficiency in Maine Young People*

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Introduction

Chronic obstructive lung disease (COLD) received close scrutiny when individuals with a deficiency in the serum alpha-1-antitrypsin concentration were found to have a high incidence of COLD. Deficiencies of serum alpha-1-antitrypsin are genetically controlled, behaving phenotypically as a Mendelian recessive. Genotypically, it has been found that there are multiple alleles (labelled E, F, G, I, M, P, S, R, V, W, X, Z) although only Z gives an abnormal phenotype consistently.[1] A low level (mean 26 mg/100 ml, range 19-36 mg/100 ml) is interpreted as the phenotypic expression of homozygosity for a deficiency gene Pi^Z allele and an intermediate level (mean 115 mg/100 ml, range 75-150 mg/100 ml) is produced by a heterozygous state. Homozygotes for the deficiency state have an incidence of COLD that is fifteen times greater than that of the general population and occurs at a younger age, the 4th or 5th decade of life, and usually in severe degree with characteristic clinical findings. The heterozygote for the Pi^Z allele in some studies has an increased tendency to develop COLD as compared to the Pi^m allele homozygote which is the normal state.

COLD occurrence continues to rise in the State of Maine and has the 4th leading rate per 100,000 population in the United States.[2] Our interest is a definition of the serum alpha-1-antitrypsin levels in Maine young people, to correlate this with their pulmonary function studies and to determine if the high incidence of COLD in Maine is due to a high incidence of alpha-1-antitrypsin deficiency.

Methods

A local high school was contacted and the project discussed with the school principal. Permission to carry out the project in the high school was obtained from the local school board. The project was then discussed with high school teachers of participating students, the students themselves and interested parents of students. Parental permission was required to participate. Consent forms, approved by the Committee for Protection of Human Research Subjects of the Maine Medical Center, explained the project in abbreviated manner and were obtained from all participants. A Respiratory Questionnaire was filled out and a 10 ml serum sample was obtained in the fasting state. Serum protein analysis was performed by the immunoassay technique of Ritchie, et al[3] and Pi typing by the immunofixation method of Alper & Johnson.[4]

Flow volume loops, expiratory and inspiratory, were performed in the usual manner as defined by Hyatt and Black[5] with a Med-Science wedge spirometer model 370. The respiratory flow and volume signals were recorded as an X-Y plot on a Tectronix 564 memory scope and photographed with a Polaroid camera. The following measurements were made for each flow-volume loop: forced vital capacity, maximum expiratory and inspiratory flow, expiratory and inspiratory flow at 75%, 50% and 25% of the forced vital capacity.

Results

Permission for students to enter the study was solicited from 295 parents; 110 (57 female and 53 male) positive responses were obtained and constituted a 37% favorable response rate.

The serum alpha-1-antitrypsin profile for the group with phenotypes MM was as follows: range 160-320 mg/100 ml., mean ± 1 standard deviation: 238.1 ± 37.3 mg/100 ml. Serum alpha-1-antitrypsin levels in the two individuals with MZ and MS genotypes were 130 and 180 mg/100 ml respectively.

The respiratory questionnaire sought information as to whether respondents had positive respiratory symptomotology, a smoking history or a family history of lung disease. Thirteen (10%) students indicated that they had trouble with breathing at exercise or on exertion. Eighty-seven (67%) of the group participated in one or more sports. Ten (8%) students who indicated trouble with breathing at exercise or exertion played sports. Twenty-seven (21%) students reported that they were smoking or had smoked cigarettes. Eleven (41%) of the smoking group noted the symptom of cough. There were equal numbers of girls (14) and boys (13) in the smoking group. The relationship between an increased number of upper respiratory tract infections (more than three colds per year), chest colds and cigarette smoking was examined. Only 7 smokers noted an increase in colds or chest colds; four positive responses in each case. A positive family history of lung disease was noted in 24 (18%). A similar incidence of tuberculosis was noted; however, tuberculosis was not equated with a positive family history of lung disease by respondents. Chest x-rays

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Table 1

Flow-Volume Expiratory/Inspiratory Data

	BOYS Real	GIRLS	P Value	BOYS	GIRLS Nondimensionalized	P Value
FVC (L)	4.48 ± 0.84	3.56 ± 0.35	< 0.005	... ...	...	
V max (L sec-¹)	9.05 ± 1.78	7.26 ± 1.06	< 0.005	2.05 ± 0.36	2.04 ± 0.28	NS
V max (Insp)	6.75 ± 1.76	5.45 ± 1.14	< 0.005	1.52 ± 0.29	1.55 ± 0.31	NS
V .75 FVC	7.32 ± 1.69	6.38 ± 1.12	> 0.01 < 0.025	1.66 ± 0.30	1.80 ± 0.30	< 0.005
V .75 FVC (Insp)	5.75 ± 1.47	4.70 ± 1.07	< 0.005	1.31 ± 0.26	1.33 ± 0.30	NS
V .50 FVC	5.06 ± 1.30	4.45 ± 1.14	NS	1.14 ± 0.25	1.26 ± 0.32	<0.01
V .50 FVC (Insp)	6.47 ± 1.67	5.12 ± 1.13	< 0.005	1.47 ± 0.29	1.45 ± 0.31	NS
V .25 FVC	2.49 ± 0.82	2.32 ± 0.60	NS	0.58 ± 0.18	0.66 ± 0.18	< 0.01
V .25 FVC (Insp)	6.15 ± 1.67	4.95 ± 1.28	< 0.005	1.41 ± 0.36	1.40 ± 0.34	NS

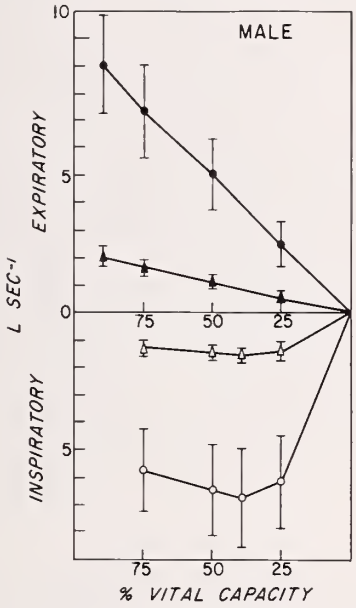

Fig. 1. Expiratory/inspiratory flow volume curves—Male.

Flow (Liters sec-1) is plotted on the ordinate & volume (per cent vital capacity) on the abscissa. Mean values are plotted with standard deviations shown. Peak expiratory/inspiratory values have two means, flow and volume. The smaller expiratory/inspiratory curves are non-dimensionalized (see text).

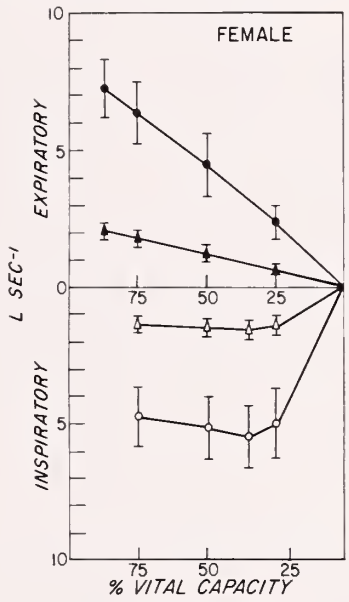

Fig. 2. Expiratory/inspiratory flow volume curves—Female.

Flow (Liters sec-1) is plotted on the ordinate & volume (per cent vital capacity) on the abscissa. Mean values are plotted with standard deviations shown. Peak expiratory/inspiratory values have two means, flow and volume. The smaller expiratory/inspiratory curves are non-dimensionalized (see text).

had been obtained on 32 (24%) of the group. The mean forced vital capacity for the boys was 4.48 L ± 0.84 and 3.56 L ± 0.35 for the girls. Inspiratory and expiratory flow data was analyzed in two ways; usually the absolute values and in a nondimensionalized form where forced vital capacity was divided into the flow data. The technique of nondimensionalization of flow data by dividing the forced vital capacity into the flow data is used to equate flow at the same relative lung volume. A similar volume adjustment has been described by Mead, et al.[6] This data is presented in Table 1. Although the flow volume loops differ significantly with the exception of points V0.50 and V0.25 FVC expired flow between adolescent boys and girls, the nondimensionalized flow-volume data shows a reverse effect with expiratory flow being significantly greater in girls than boys except in the flow maxima which is not different. These curves are illustrated in Figures 1 and 2.

TABLE 2

	AGE	REAL BOYS	REAL GIRLS	P VALUE	NONDIMENSIONALIZED BOYS	NONDIMENSIONALIZED GIRLS	P VALUE
HEIGHT (INCHES)	14	66.4 ± 3.6 (N = 13)	64.5 ± 2.1 (N = 26)	NS			
	15	68.3 ± 2.9 (N = 19)	65.5 ± 1.7 (N = 16)	< 0.005			
	16	70.0 ± 2.5 (N = 16)	65.6 ± 2.9 (N = 14)	< 0.005			
WEIGHT (POUNDS)	14	140.8 ± 38.7	128.7 ± 18.0	NS			
	15	139.3 ± 25.5	129.3 ± 16.0	NS			
	16	156.0 ± 22.1	137.2 ± 20.4	.01 < P < 0.25			
VITAL CAPACITY (LITERS)	14	3.8 ± 0.90	3.4 ± 0.37	NS			
	15	4.5 ± 0.80	3.6 ± 0.35	<0.005			
	16	4.7 ± 1.3	3.8 ± 0.27	.01 > P > 0.005			
$\dot{V}$ MAXIMA EXPIRATORY (LITERS SEC^{-1})	14	7.7 ± 1.5	7.2 ± 1.0	NS	2.1 ± 0.52	2.1 ± 0.28	NS
	15	8.6 ± 1.7	7.1 ± 0.91	<0.005	1.9 ± 0.28	2.0 ± 0.27	NS
	16	9.6 ± 2.7	7.6 ± 1.2	.01 > P > 0.005	1.9 ± 0.55	2.0 ± 0.30	NS
$\dot{V}$ MAXIMA INSPIRATORY (LITERS SEC^{-1})	14	5.3 ± 1.1	5.6 ± 1.3	NS	1.4 ± 0.30	1.6 ± 0.34	.01 < P < .025
	15	6.9 ± 1.8	5.3 ± 0.83	<0.005	1.5 ± 0.25	1.5 ± 0.23	NS
	16	7.0 ± 2.4	5.3 ± 0.97	<0.005	1.5 ± 0.51	1.4 ± 0.25	NS
$\dot{V}$ 0.75 FVC EXPIRATORY (LITERS SEC^{-1})	14	6.3 ± 1.6	6.2 ± 1.0	NS	1.7 ± 0.31	1.8 ± 0.30	NS
	15	6.8 ± 1.1	6.2 ± 1.1	NS	1.5 ± 0.23	1.7 ± 0.28	.01 < P < .025
	16	7.6 ± 2.4	6.8 ± 1.3	NS	1.6 ± 0.50	1.8 ± 0.33	NS
$\dot{V}$ 0.75 FVC INSPIRATORY (LITERS SEC^{-1})	14	4.6 ± 1.3	4.5 ± 1.3	NS	1.3 ± 0.31	1.5 ± 0.33	.025
	15	5.8 ± 1.3	4.5 ± 0.72	<0.005	1.3 ± 0.20	1.3 ± 0.19	NS
	16	6.1 ± 2.0	4.4 ± 0.88	<0.005	1.3 ± 0.45	1.2 ± 0.23	NS
$\dot{V}$ 0.5 FVC EXPIRATORY (LITERS SEC^{-1})	14	4.2 ± 1.3	4.3 ± 1.0	NS	1.1 ± 0.26	1.3 ± 0.30	NS
	15	4.8 ± 0.79	4.2 ± 1.0	NS	1.1 ± 0.23	1.2 ± 0.30	NS
	16	5.4 ± 1.8	4.9 ± 1.4	NS	1.1 ± 0.37	1.3 ± 0.38	NS
0.5 FVC INSPIRATORY (LITERS SEC^{-1})	14	5.2 ± 1.0	5.3 ± 1.3	NS	1.4 ± 0.29	1.6 ± 0.33	NS
	15	6.4 ± 1.7	5.0 ± 0.77	<0.005	1.4 ± 0.26	1.4 ± 0.21	NS
	16	6.8 ± 2.4	4.7 ± 1.1	<0.005	1.4 ± 0.51	1.2 ± 0.25	NS
$\dot{V}$ 0.25 FVC	14	1.9 ± 0.84	2.2 ± 0.60	NS	0.54 ± 0.19	0.67 ± 0.17	.01 < P < .025

TABLE 2

	AGE	REAL BOYS	GIRLS	P VALUE	NONDIMENSIONALIZED BOYS	GIRLS	P VALUE
EXPIRATORY (LITERS SEC^{-1})	15	2.5 ± 0.61	2.3 ± 0.60	NS	0.58 ± 0.16	0.65 ± 0.19	NS
	16	2.6 ± 0.92	2.5 ± 0.60	NS	0.56 ± 0.22	0.65 ± 0.20	NS
$\dot{V}$ 0.25 FVC INSPIRATORY (LITERS SEC^{-1})	14	4.8 ± 1.1	5.1 ± 1.5	NS	1.3 ± 0.24	1.5 ± 0.38	NS
	15	6.5 ± 1.9	4.9 ± 0.93	<0.005	1.4 ± 0.29	1.3 ± 0.25	NS
	16	6.4 ± 2.1	4.6 ± 1.1	<0.005	1.4 ± 0.63	1.2 ± 0.26	NS

The boys and girls were further subdivided by age into groups of 14, 15, 16 year olds (Table 2). Height did not vary between 14 year old boys and girls; however, boys age 15 and 16 were significantly taller than comparably aged girls. Sixteen year old boys weighed significantly more than 16 year old girls, weight did not vary significantly in the other two groups of boys and girls. As a group, 14 year old boys and girls did not vary significantly in respiratory parameters measured. Among the 15 and 16 year old boys and girls, the respiratory values increased with age and was significantly greater in boys than girls with the exception in expiratory flow at 0.75, 0.5 and 0.25 volume remaining in the forced vital capacity. When the respiratory data was nondimensionalized $\dot{V}$ maxima, expiratory and inspiratory showed nonsignificant variation with exception of inspiratory $\dot{V}$ maxima in 14 year olds. Other significant nondimensionalized flow variation occurred in the 15 year olds with the expiratory V 0.75 FVC and inspiratory $\dot{V}$ 0.75 FVC and expiratory $\dot{V}$ 0.25 FVC among the 14 year old group. When smokers were compared, there was no difference.

DISCUSSION

This study sought to define the serum alpha-1-antitrypsin profile and pulmonary function in a group of normal young individuals. It is unfortunate that our group is small and that significant data regarding the alpha-1-antitrypsin deficiency syndrome cannot be obtained; however, certain inferences can be made. Recently, Pierce and coworkers reported on antitrypsin phenotypes from 2,285 blood donors in St. Louis. The frequency of occurrence of the Pi^Z allele was much lower than previously reported in Scandinavian test groups.[7] Our small group has a Pi^Z allele frequency 2.5 times smaller and a Pi^S allele frequency of 7.5 times lower than the St. Louis group; however, because our group is small, random variation could account for these findings. The serum alpha-1-antitrypsin level for our heterozygotes is consonant for those levels reported for other heterozygotes.[8]

Using 95% confidence limits, we can state with reasonable certainty that the incidence of the Pi^Z allele in this population is 2.5% or less. Therefore, 0.025 x 0.075 = 0.000625, less than 0.07% of the population would be expected to be homozygous for this condition. Extrapolating for the entire Maine population we are 95% certain that there are less than 625 of these people in the state.

The student cigarette smokers in our group (21%) is comparable to that of students entering Drexel University (23.7%) over an eleven year period.[9] The Drexel University data shows, however, that over the eleven year period a decrease occurred to 14.6% from 32.9% in cigarette smoking. The high level of cigarette smoking in young adolescents is disturbing because there are more smokers among the early high school students in this study than there were in college freshmen studied several years ago. This implies an increase in smoking in the young. Also, the habit is distributed equally among boys and girls portending an equal distribution of COLD and carcinoma of the lung among the sexes. Cough (41%) in the smoking group suggests bronchial irritation despite lack of objective evidence of functional impairment. The effect of cigarette smoking on lungs is widespread. Infants had a double risk of an attack of pneumonia or bronchitis in the first year of life if their parents smoked.[10] Cough in school children, 6-14 years, was associated with the smoking habits of the parents. The lowest incidence was when both parents were non-smokers and the highest was when both parents smoked.[12] We feel it is important to underscore the evidence pointing to cigarette smoke as playing a major role in the genesis of COLD and that the process starts at a young age. Furthermore, the high incidence of smoking in young adolescents is significant and represents failure of present anti-smoking programs. Failure of educational programs to influence smoking and drug behavior is reported[13,14,15] and indicates the need for more innovative programs.

The accepted manner of presentation of predicted respiratory data is separation into male and female and grouping by age and height.[16] If maximum expiratory flow values are nondimensionalized then ab-

TABLE 3*

	MALE (N = 36)		FEMALE (N = 38)	
	Real	*Nondimensionalized*	*Real*	*Nondimensionalized*
Vital Capacity (L)	5.24 ± 0.65	. . .	3.54 ± 0.46	. . .
V Maximum (Expiratory L Sec^{-1}) SL	10.5 ± 1.67	2.02 ± 0.33	6.74 ± 1.00	1.92 ± 0.29
$V^{0.5}$vc (Expiratory V0.5vcL Sec^{-1}) SL	4.54 ± 1.28	0.88 ± 0.25	4.14 ± 1.10	1.19 ± 0.33

*Age group 20-29 years

solute value differences as a function of age, sex and body size become considerably smaller. This relationship continued through age 20-29 with decreased flow at the 50% vital capacity level in males compared to females (Table 3).

Despite larger vital capacities in the adult group, expiratory flow maxima are the same and decreased at the 50% vital capacity level in both male and female. This suggests that pulmonary function attains maximum level early in life in the second decade and deterioration of function may begin within the third decade. Although maximum expiratory flow is volume dependent, nondimensionalization of expiratory flow, that is dividing the flow by the forced vital capacity, gives a constant flow unit for males and females. This further suggests that the classic practice of separating male and female pulmonary function is artificial and that the nondimensionalized flow would be more meaningful.

SUMMARY

This study suggests that serum alpha-1-antitrypsin deficiencies in Maine young people are less frequent than in other populations. Determinations of serum alpha-1-antitrypsin levels is not a practical screening method for COLD.

Smoking in adolescents is significant and anti-smoking programs in the grade schools are ineffective. The need for more innovative programs is pointed out.

Respiratory flow data shows minor differences between boys and girls when the data is nondimensionalized to show respiratory unit function rather than lung volume function. Maximal expiratory flow is achieved within the mid-second decade and begins to decrease in the third decade.

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Thrombotic Complications of Central Vein Hyperalimentation

Irving Kron, M.D., Joel Johnson, M.D. and Saul Katz, M.D.*

Abstract

Central vein thrombosis is an infrequently reported complication of intravenous hyperalimentation. Venograms have been useful in documenting its presence and extent in four patients. Central vein thrombosis should be considered in the hyperalimented patient when catheter replacement becomes difficult, or when superior vena cava syndrome or pulmonary embolus occurs.

Intravenous hyperalimentation has achieved widespread use and application since its introduction by Dudrick in 1968.[1] Complications have included catheter sepsis,[2] difficulty with catheter placement,[3] and metabolic abnormalities.[4]

Central vein thrombosis secondary to intravenous hyperalimentation was originally thought not to be a problem because of vessel size and high flow rate.[1] However, reports relating autopsy data have documented subclavian vein thrombosis as well as pulmonary emboli of presumed central vein origin.[6,7,8,9] We have encountered four cases of central vein thrombosis secondary to intravenous hyperalimentation. One was complicated by pulmonary emboli. All have been documented by venogram.

Methods

Polyethylene catheters† were placed percutaneously via the subclavian or internal jugular route under strictly aseptic conditions. Prior to institution of hyperalimentation, position of the catheter in the superior vena cava was confirmed by chest x-ray. Daily intravenous tubing changes as well as every other day dressing changes were performed by the nursing staff according to the department of surgery protocol.

Case Reports

Case 1. This 47-year-old male underwent splenectomy, partial pancreatectomy, and colectomy for pancreatic abscess. He was supported by intravenous hyperalimentation requiring several cannulations of both subclavian veins without apparent complication. The patient returned one year later with a chronic pancreaticocutaneous fistula. It was elected to treat this with intravenous hyperalimentation. Several attempts at subclavian catheterization were unsuccessful as the catheter could not be threaded centrally. A superior vena cavagram revealed bilateral innominate and proximal subclavian vein occlusion. The only demonstrable flow was through the right internal jugular vein (Fig 1). The patient was treated with an oral elemental diet and eventually discharged.

Fig. 1

Case 2. A 74-year-old white male was readmitted with a small bowel obstruction one month after transabdominal hiatus hernia repair. Because of cachexia, total parenteral nutrition was initiated prior to laparotomy and continued for a total of ten days. The patient returned ten days after discharge with two days of progressive swelling and pain in the left arm. Venograms demonstrated complete occlusion of the left subclavian vein with collateral flow around the shoulders and base of the neck (Fig 2). The right subclavian vein was free of thrombus. The arm improved with intravenous heparin therapy.

Case 3. A 56-year-old cook had lost fifty pounds and was unable to swallow clear fluids due to an esophageal stricture following proximal gastrectomy complicated by an anastomic leak and subphrenic abscess. Following odontectomy, the patient suffered a myocardial infarction and esophageal reconstruction was deferred. Intravenous hyperalimentation was initiated and the catheter replaced several times because of fever. Catheter cultures were negative. An initial lung scan was within normal limits. A repeat study revealed a large perfusion defect in the left lower lobe (Fig 3). Lower extremity venograms did not demonstrate evidence of thrombus. Inferior vena caval interruption was considered until upper extremity venograms were obtained which revealed bilateral subclavian and innominate vein thrombosis (Fig 4). The patient was temporarily anticoagulated until central lines were removed. He was discharged following esophageal dilatation and placement of a feeding tube. Reconstruction will be done at a later date.

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†Deseret Intracath 8 inch polyethylene catheter #3162. Deseret Pharmaceutical Co., Inc., Sandy, Utah 84070.

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Fig. 2

Fig. 4a

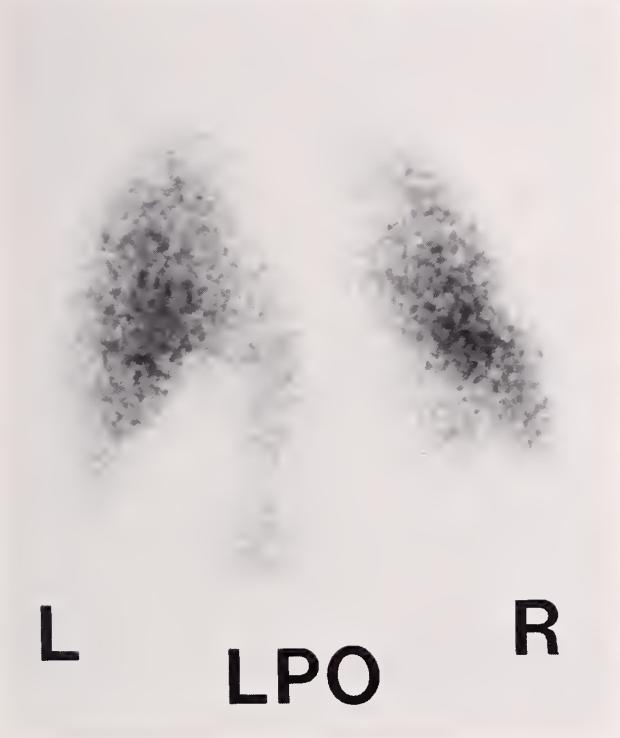

Fig. 3

Fig. 4b

Case 4. A 76-year-old man was treated with hyperalimentation following esophagogastrectomy. His postoperative course was complicated by gastric stasis and an esophagopleuro-cutaneous fistula. The catheter was replaced several times because of unexplained fever. After six weeks, he developed a superior vena cava syndrome. Bilateral upper extremity venograms revealed obstruction of both subclavian veins. Fluid and nutritional maintenance became more difficult and he died of dehydration and malnutrition following development of a massive right pleural effusion.

Discussion

Central vein thrombosis following intravenous hyperalimentation has been found at post mortem examination although documentation during life has seldom been reported.[6,7,8,9] The appearance of four cases in our institution within a brief period suggests that central vein thrombosis occurs more commonly than has been suspected.

Since the hypertonicity of hyperalimentation preparations can induce thrombosis of small peripheral vessels, the use of high flow central veins was proposed to avoid this effect by dilution of the sclerotic solution.[1,10] Damage to the intima may also

be caused by multiple venous punctures. Thin sheaths of fibrin can be found on central catheters of any composition and may act as a nidus for the propagation of clot.[8] Additionally, malposition of the catheter, causing partial venous obstruction and intimal trauma, has also been reported as a cause of thrombosis.[5] It is apparent that the presence of a hyperalimentation line may add stasis and intimal damage to the patient already hypercoagulable from injury, sepsis, or dehydration. Virchow's triad is therefore fulfilled and thrombosis may ensue.

The critical value of demonstrating central vein thrombosis is evident from our patients. In Case #1, the only upper extremity outflow was shown to be through the right internal jugular vein. If this had been catheterized after other sites proved unsatisfactory, a superior vena cava syndrome could have developed. In Case #3, venograms showed the source of emboli to be the upper rather than the lower extremities. Long term anticoagulation was therefore not recommended. Inferior vena cava interruption which had been considered in this patient would have been inappropriate. Removal of the catheter and alimentation by an alternate route was successful in preventing further complications in both of these patients.

Our experience indicates that central vein thrombosis should be considered when catheter placement becomes difficult. It is probably the etiology when edema of the upper arm or superior vena cava syndrome appears in a patient on intravenous hyperalimentation. In addition, pulmonary embolus, in the absence of demonstrable ileo-femoral thrombosis in a hyperalimented patient, should raise suspicion of central vein thrombosis. We would recommend removal of the offending catheter and bilateral venograms prior to insertion of another indwelling line in the opposite side.

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the possible reasons discussed. Early surgical therapy and adjuvant radiotherapy may improve survival statistics. The high incidence of bilateral metachronous involvement with breast cancer and a high incidence of previously treated malignancy is noted in this series, suggesting further areas for investigation.

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Editorials

Second Thoughts on Second Opinions

It is strange how so traditional a part of everyday practice as seeking consultation could be a mechanism of third parties to reduce their cost of doing business. The idea is if subscribing patients heed the more conservative of two opinions money will be saved for the stockholders or taxpayers, as the case may be. In a word, the less surgery, the better. Or is it?

What about the patient's well-being? Who can say that a second opinion is necessarily wiser than the first? Where, indeed, is the evidence that less surgery will have a salubrious effect on the nation's health? Certainly when it comes to cancer, vastly more people perish from the lack of an early operation than an unnecessary one.

But proven or unproven, third party second opinion programs are upon us. For society they may just cost more than they save. For the profession they come as an affront, a subversion of the traditional open consultative process which illuminates the problem and educates its participants. We are stung by the thought that the second opinion maker is not necessarily a surgeon or even an M.D.! And we chafe over the requirement that the second doctor, if asked, must conceal the very fact of the second opinion request.

The consultative process wasn't invented by the government. At the bedside, in the conference room, in the corridors of every hospital in the state we have for years given *free* advice, consultation and second opinions. Let us continue to do so and even extend the offer of free consultation to those few patients who want a second opinion in the office setting.

Someone needs to speak up for the honor of the profession, again the target of that resilient canard that it is private gain rather than personal concern that motivates the doctor. We know otherwise; it is our responsibility to care for our patients so that they know too.

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Maine's Medical Resource Assets

This spring a New York surgical travel club visited the State instead of their usual annual trip to a major clinic in Europe or North America. Their purpose was the exchange of ideas among surgeons and their expectations were relaxed regarding the State of the art in a predominantly rural state. At the end of the three day visit, there was open amazement at the range and excellence of medical and surgical resources available to the people of Maine. Effective Emergency Medical Services, arrangements for inter-hospital consultation and transfer of neonatal and trauma cases, and coordinated oncology study programs were no less impressive to this group than successful renal transplant and cardiac surgery programs, functioning problem-pregnancy programs, regional radiation therapy programs, a State-wide burn care program, and effective programs of continuing physician education. The ready implementation of advances in medical care throughout the State drew the envy of urban surgeons with more entrenched bureaucrats and less enlightened trustees. Let us count our blessings which by comparison with over-populated urban areas are too frequently taken for granted.

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Chronic Hepatitis

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ABSTRACT

The clinical manifestations of chronic hepatitis are of limited diagnostic use. Diagnosis must be made by liver biopsy. The disease is classified as chronic persistent or chronic active hepatitis. The prognosis for chronic persistent hepatitis is excellent, and no treatment is required. Chronic active hepatitis may progress to cirrhosis and is associated with a poor prognosis if untreated. Recognized causes of chronic active hepatitis are hepatitis-B virus infection, post-transfusion hepatitis not associated with hepatitis-B virus, and certain drugs. For drug-induced hepatitis, discontinuation of the medication is indicated. For other types of chronic active hepatitis the recommended treatment is prednisone 10 mg and azathioprine 50 mg daily.

Chronic hepatitis is an inflammatory liver disease continuing for at least six months without improvement. The diagnosis may be suspected from symptoms or altered liver function tests and is confirmed by a liver biopsy. The disease may occur alone or accompany other illnesses. Treatment varies according to the cause and type of histological changes and usually results in suppression of the manifestations of the disease rather than elimination or eradication of its cause.

An advanced stage of this disease was first described in the early 1950's. Additional clinical and pathological observations were added in subsequent years. This increased knowledge was compromised, however, by the introduction of a large number of clinical, morphological, and etiological descriptive terms—each one allegedly more accurate than its predecessors. In addition, numerous uncontrolled or anecdotal reports of treatment were published. The uncertainty of treatment of chronic hepatitis was matched by the confusion of the nomenclature used to describe this disease.

CLASSIFICATION

In 1968 a new classification was proposed that divided chronic hepatitis into two groups.[1] The first category, termed *chronic persistent hepatitis,* was characterized by chronic inflammatory infiltration of the portal areas, preservation of lobular architecture, and absence of fibrosis with or without the features of acute hepatitis. The prognosis of these patients has proved to be excellent, and treatment is not required.[2] The second category, termed *chronic aggressive hepatitis,* was characterized by chronic inflammatory infiltration involving the portal areas with direct extension into the lobule, necrosis of the cells at the edge of the lobule nearest the portal area (piecemeal necrosis), and increased fibrosis with or without the features of acute hepatitis. Patients with liver disease of this histological description had a guarded prognosis and frequently developed cirrhosis, particularly if the inflammation and necrosis at the edge of the lobule were severe. This description as it related to the risk of developing cirrhosis overstated the importance of piecemeal necrosis and omitted mention of more extensive necrosis where cell collapse extended beyond the lobule between portal triads or portal triads and central veins (bridging necrosis).

The most recent classification of chronic hepatitis was developed by the International Association for the Study of the Liver and has been accepted by the World Health Organization.[3] The term chronic persistent hepatitis is retained. Chronic aggressive hepatitis is called *chronic active hepatitis*, and the morphological description now includes the additions and corrections mentioned above. Assignment of cases with ambiguous histological changes to the appropriate category and identifying those mild cases of chronic active hepatitis that may heal without therapy remains problematic.

CLINICAL COURSE

The clinical presentation of chronic hepatitis is an unreliable guide to diagnosis. Patients with chronic persistent hepatitis may feel well or experience fatigue, abdominal discomfort, or failure to gain weight. Serum levels of transaminases (SGOT, SGPT) will be moderately elevated while other liver function tests, especially serum globulin, will be normal. Chronic active hepatitis may be asymptomatic or may have symptoms related to the hepatic illness, including fatigue, anorexia, nausea, weight loss, abdominal discomfort, arthralgias, fever, acne, amenorrhea, and, if the disease is more advanced, easy bruising, epistaxis, edema, ascites, hematemesis from esophageal varices, and portal-systemic encephalopathy. Additional symptoms may occur that are characteristic of several other idopathic

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disorders including ulcerative colitis, thyroiditis, Cushing's syndrome, pericarditis, myocarditis, hemolytic anemia, glomerulonephritis, and renal tubular acidosis. These diseases may proceed, occur with, or follow the onset of chronic active hepatitis. Significant laboratory abnormalities include high levels of serum transaminases and an increased serum globulin. With more advanced disease there may be an elevation of the serum bilirubin and alkaline phosphatase and a fall in the serum albumin.

The course of the disease is unpredictable. Signs and symptoms fluctuate with episodes of active disease. Recurring hepatic necrosis, reflected by malaise, jaundice, and deteriorating laboratory studies, leads ultimately to cirrhosis. Although symptoms may remit, the disease is, with few exceptions, irreversible. Death from hepatocellular failure with or without portal hypertension frequently occurs in the first few years after the diagnosis is made. The prognosis of the untreated disease is poor, with 50% of the patients surviving less than five years.[4,5] The disease may "burn out," however, and there are many examples of patients who have lived more than ten years.[6]

Etiology

Of the many known or suspected causes of chronic hepatitis, viral infections are currently the most important. Infection with hepatitis-A virus (HAV) has been considered a cause of chronic hepatitis but is not documented. The recent introduction of serological techniques to identify HAV antigens and antibodies may clarify this question. Infection with hepatitis-B virus (HBV) can now be detected with sensitive radioimmunoassays for HBV antigens and antibodies. These serological techniques, based upon discovery of the hepatitis B surface antigen (HBsAg) by Blumberg in 1967, have documented that infection with HBV may lead to chronic hepatitis. The HBV antigen and antibody systems are reviewed in detail elsewhere.[7]

In 1972, a new group of precipitating antigens designated as *e* was identified in HBsAg positive serum.[8] The antigen is distinct from surface (HBsAg) and core (HBcAg) antigens and is never detected in HBsAg negative serum. It is not part of the hepatitis-B virion. The presence of the e antigen correlates with an increased level of DNA polymerase activity and an elevated number of Dane particles[9] and is a guide to the relative infectivity of HBsAg positive serum.[10] It has been suggested that the presence of the e antigen in acute HBV infection identifies those patients who will progress to chronic hepatitis.[11] There is ample evidence to confirm that correlation. In the individual patient, however, the e antigen does not have prognostic value. The HBeAg positive patient may heal the acute infection completely.[9,12] Antibody to e antigen appears to indicate a low level of infectivity and is found frequently in patients who have no histological hepatic abnormalities (healthy carrier state).[9] Further studies of the behavior of this antigen antibody system will undoubtedly increase our understanding of HBV infections.

Other viral-like agents may cause chronic hepatitis. In spite of screening blood donors for HBV antigens, there has been only a moderate reduction in the frequency of post-transfusion hepatitis. Post-transfusion hepatitis now appears to be an infection unrelated to the HAV, HBV, Epstein-Barr virus, or cytomegalovirus and has been described by the awkward term "non-A, non-B, post-transfusion hepatitis."[13] There is also evidence for the existence of this or a similar infection causing clinical or nonclinical illness in persons who have not had blood transfusions.[14] The natural history of non-A, non-B, post-transfusion hepatitis has been described in patients who have undergone cardiac surgery. Chronic persistent hepatitis, chronic active hepatitis, or cirrhosis developed in ten of forty-four cases. In a similar group of patients given immune serum globulin preoperatively the incidence of post-transfusion hepatitis was reduced as was the incidence of progression of post-transfusion hepatitis to chronic liver disease.[15]

Many different drugs alter hepatic function and histological appearance, but to date only a few have been casually related to hepatitis. Those drugs associated with chronic active hepatitis include methlydopa,[16] dantrolene,[17] isoniazid,[18] aspirin,[19] and oxyphenisatin.[20] Aspirin in high doses has produced chronic active hepatitis but only in patients with systemic lupus erythematosus.

Oxyphenisatin was formerly marketed as a laxative, either alone or in combinations, one of which was with a detergent, dioctyl sodium sulfosuccinate. Since chronic active hepatitis developed in patients receiving oxyphenisatin alone or receiving oxyphenisatin in combination with ingredients other than dioctyl sodium sulfosuccinate, and since patients with liver disease responded abnormally to a challenge with oxyphenisatin alone, oxyphenisatin was identified as hepatotoxic and removed from the market.[20] Dioctyl sodium sulfosuccinate, however, may not have been innocuous. Chronic active hepatitis was more frequent in patients using the combination preparation than in those using oxyphenisatin alone, suggesting that dioctyl sodium sulfosuccinate contributed to the hepatotoxicity.[21] Dioctyl calcium sulfosuccinate, a similar detergent, in combinations with danthron (Doxidan®) has been associated with chronic active hepatitis and leukopenia in one case report.[22] Even the mechanism of stool softening by dioctyl sodium sulfosuccinate, formerly attributed solely to surface-active properties, may include stimulation of fluid secretion by the small bowel and colon.[23] These detergents are clearly active biological agents, and their use may increase

the risk of hepatotoxicity from other drugs.

Withdrawal of the offending agent is the appropriate treatment in drug-associated chronic hepatitis. If the histological changes have not progressed to cirrhosis, the disease subsides. Individuals investigating or prescribing drugs should be suspicious of any abnormality of liver function in recipients because drugs other than those listed above may be associated with chronic hepatitis.

In view of the many immunological abnormalities in chronic hepatitis, a primary autoimmune phenomenon has been considered as a possible cause. Cell mediated hypersensitivity is suggested by the altered response of peripheral lymphocytes to phytohemagglutinin and by tissue infiltration of lymphocytes and plasma cells, characteristic features of a rejection reaction. The features of antibody mediated disease are united in the description of lupoid hepatitis.[24] This entity was once proposed as a specific form of autoimmune chronic hepatitis distinct from cases of viral, drug, or unknown causes. Lupoid hepatitis was characterized by a positive lupus erythematosus (LE) cell test in association with an elevated serum globulin, antibodies to various non-organ specific tissues, and autoimmune-like diseases such as ulcerative colitis or thyroiditis. A discriminating comparison of LE positive patients with LE negative patients did not demonstrate, however, that these groups differed clinically, biochemically, or histologically. It was concluded that the positive LE test indicated more active inflammation rather than a specific cause of liver disease.[25] Disturbed or inappropriate immunological responses possibly perpetuate chronic hepatitis, but there is no evidence that they are a primary initiating agent.

To summarize, the etiologies of chronic hepatitis include hepatitis-B, the agent or agents of non-A, non-B hepatitis, and certain drugs. In spite of this list, the cause of the majority of the cases of chronic hepatitis is unknown.

Two diseases with which chronic active hepatitis may be confused are alcoholic liver disease and Wilson's disease. The former is identified by the history, when obtainable, of excessive alcoholic intake as well as certain histological features on liver biopsy. The latter is distinguished from both chronic active hepatitis and alcoholic liver disease by Kayser-Fleischer rings and a low level of serum ceruloplasmin. Alpha$_1$-antitrypsin deficiency has also been associated with chronic active hepatitis.[26] Rarely, primary biliary cirrhosis may be confused with chronic active hepatitis but can usually be distinguished by high levels of serum alkaline phosphatase and immunoglobulin-M, the antimitochondrial antibody, and the lack of response to steroid therapy. Although steroids are contraindicated in primary biliary cirrhosis, their short-term

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Tablets
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DESCRIPTION Each tablet of PERCOCET®-5 contains 5 mg oxycodone hydrochloride (WARNING: May be habit forming), 325 mg acetaminophen (APAP).

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone or acetaminophen.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCOCET®-5, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCOCET®-5 is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCOCET®-5 should be cautioned accordingly.

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCOCET®-5 may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

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Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus.

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use may be helpful in distinguishing between these two diseases.[27]

Treatment

At present the use of systemic steroids with or without azathioprine is indicated in the treatment of chronic active hepatitis. This concept was first suggested in a well-controlled Danish trial of prednisone in cirrhosis.[28] Those patients doing best were young women with nonalcoholic cirrhosis and with a high serum globulin level, a group which one might suspect included patients with advanced chronic active hepatitis. In 1971 a randomized, controlled study undertaken to determine if steroids were effective in the treatment of chronic hepatitis was reported.[5] In that trial 22 patients were treated and 27 served as controls. The trial was discontinued after six years because of the striking effect of steroid therapy. The mortality in the control group was 55%, as compared to 14% in the treated group. These results were subsequently confirmed.[29,30]

Summerskill and his colleagues at the Mayo Clinic have conducted a continuing, prospective, controlled, double-blind randomized trial of treatments of chronic hepatitis for ten years.[29,31] They recognized in their patients a broad spectrum of histological changes, ranging from mild chronic active hepatitis to severe chronic active hepatitis with cirrhosis, and therefore decided to use the more inclusive term, chronic active liver disease. They emphasized the importance of certain histological features discussed above and confirmed the therapeutic value of prednisone. They reported that azathioprine alone is of no value, but that azathioprine can be combined with prednisone to reduce the amount of prednisone needed to treat the disease, and that daily prednisone therapy is preferable to every-other-day therapy.

Their four treatment programs (placebo, azathioprine, prednisone, or prednisone combined with azathioprine) were continued until side effects necessitated discontinuing the medication, treatment failure occurred, or the patient entered remission. Remission was defined as the absence of symptoms and return to normal activity, return of all liver function tests to normal, except for an SGOT up to twice normal, and a follow-up liver biopsy appearing normal or showing either mild inflammation consistent with chronic persistent hepatitis or inactive cirrhosis. When a patient entered remission, medication was tapered over a six-week period and discontinued. If the disease relapsed (SGOT greater than three times normal) the same treatment was reinstituted. The best treatment programs were either prednisone, 50 mg daily, tapered over a month to a maintenance of 20 mg daily; or prednisone, 30 mg daily, tapered over a month to a maintenance dose of 10 mg daily in combination with azathioprine 50 mg daily. Two years of treatment with either of these regimens led to remission in symptoms and clinical features in 80% of the patients and to histological remission in 60%. The sequence of events in the responders was typified by remission of symptoms in two to three months, remission in biochemical abnormalties in three to six months, and histological remission in six to twenty-two months.

A recent analysis of these three controlled trials identified avoidable and unavoidable deficiencies in each.[32] While indicating that the conclusions reached in these trials were similar, the authors concluded that the benefit for steroid therapy had been established only for those patients who were symptomatic, who were HBsAg negative, and who had severe histological abnormalities. Appropriate management of the asymptomatic patient with chronic hepatitis is still to be determined.[33] The HBsAg positive patient appears to differ from those who are HBsAg negative. There is a predominance of males, an older average age, and a lower incidence of immunoserological markers.[34] Since many patients with HBsAg positive acute hepatitis clear the antigen as chronic hepatitis develops and become HBsAg negative,[35] the difference between these two groups may indicate variation in host response rather than specific cause. Whether HBsAg positive patients with chronic hepatitis should be treated is unclear. A retrospective study suggested that the progress of the disease was slow and that steroid therapy was probably of benefit.[36] In the Mayo Clinic experience, the treated HBsAg positive group did have a better survival than a control placebo group but did not respond as frequently as the HBsAg negative patients.[34] There is currently a need for a controlled trial of prednisone treated and untreated HBsAg positive patients. Until such a study is completed it seems best to treat the symptomatic HBsAg positive patient.

The side effects of prednisone when taken chronically by these patients have been significant. In 67% of the patients receiving 20 mg of prednisone daily, major side effects such as diabetes, cataracts, and osteoporosis with aseptic necrosis of the hip or vertebral collapse occurred. In those receiving the drug for more than twelve months, 20% experienced such severe side effects that the drug had to be discontinued. In those patients receiving a combination of prednisone 10 mg and azathioprine 50 mg daily, the side effects of the drugs were considerably less frequent. Since this combination therapy is as effective as 20 mg of prednisone alone in inducing remission, it has been proposed as the best current treatment.[31]

Conclusion

Optimal therapy of chronic hepatitis is still in the developmental stages. Prednisone was shown to be of therapeutic value only seven years ago and prednisolone with azathioprine only five years ago. In contrast to the recognized physiological effects of

certain drugs (for example, the reduction of gastric acid secretion by cimetidine) the pharmacodynamics of prednisone in chronic active hepatitis are not understood. Prednisone may alter the actions of the causative agent or suppress immunological phenomena. In the future, more innovative therapeutic regimens aimed at altering or eradicating the causative agent can be anticipated. Some new therapies have been reported, including the use of transfer factor,[37] interferon,[38] and antiviral agents.[39] Although of greatest interest, these have not yet proved beneficial.

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President

Maine Medical Association

1978-1979

FRANCIS I. KITTREDGE, M.D.

Francis I. Kittredge, M.D., of Bangor, Maine, became the 129th President of the Maine Medical Association at the 125th annual session banquet on June 12, 1978. He served as President-elect of the Maine Medical Association from 1977-1978.

Dr. Kittredge was born in Philadelphia, Pennsylvania on November 8, 1934, son of Francis I. and Mary M. Kittredge. He was graduated from the University of Notre Dame in 1956 and received his medical degree from Temple University School of Medicine in 1959. He served in the U.S. Army as a Captain from 1959 to 1962, interned at the Martin Army Hospital in Georgia, served a residency in Neurology at the Pennsylvania Hospital and took a postgraduate course at Temple University School of Law. Dr. Kittredge located in Bangor in 1972 where he is affiliated at the Eastern Maine Medical Center (Chief of Neurology), St. Joseph Hospital and J. A. Taylor Osteopathic Hospital (consulting).

He is a member of the Penobscot County Medical Association, the Maine Medical Association, the American Medical Association and the M.M.A. Committee on Legislation.

Dr. Kittredge is a member of the Commission to Revise the Laws Relating to Medical and Hospital Malpractice Insurance, Vice Chairman of the Joint Underwriting Association, Associate Editor of the Journal of Legal Medicine, member of the Maine State Bar, Federal Bar, American and Maine Bar Associations, American Trial Lawyers Association and Maine State Trial Lawyers Association.

Executive Committee Members Elected at the 125th Annual Session of the Maine Medical Association

Rockport, Maine June 10-13, 1978

President
FRANCIS I. KITTREDGE, M.D.
Bangor

President-elect
BRINTON T. DARLINGTON, M.D.
Augusta

Second District
WILLIAM H. MAXWELL, M.D.
Portland

Fourth District
O. THOMAS FEAGIN, M.D.
Augusta

Fifth District
DAVID L. PHILLIPS, M.D.
Rumford
Executive Committee Chairman

Seventh District
GILBERT R. GRIMES, M.D.
Lewiston

Ninth District
HARRY M. HELFRICH, JR., M.D.
Presque Isle

Speaker of the House
GEORGE W. BOSTWICK, M.D.
Newcastle

Dr. Brinton T. Darlington was elected President-elect; and Dr. George W. Bostwick, Speaker of the House. The following physicians were elected to the Executive Committee: Dr. William H. Maxwell, Second District (1978-1981); Dr. O. Thomas Feagin, Fourth District (1978-1981); Dr. David L. Phillips, *Chairman* of the Executive Committee (1978-1979); Dr. Gilbert R. Grimes, Seventh District (1978-1980), to complete Dr. Ross W. Green's unexpired term; and Dr. Harry M. Helfrich, Jr., Ninth District (1978-1981).

DR. DARLINGTON, of Augusta, was born in Olean, New York on January 7, 1922, son of J. Leon and Martha T. Darlington. He was graduated from Ohio University in 1943 and received his medical degree from State University of New York Upstate Medical Center, Syracuse in 1945. He interned at St. Luke's Hospital in Cleveland, Ohio and served a residency at the U.S. Marine Hospital in Staten Island. In 1952, he located in Augusta.

He is a member of the Kennebec County Medical Association, the Maine Medical Association, the American Medical Association, and is a member of the Liaison Committee between the Maine Bar Association and the Maine Medical Association, the M.M.A.'s Committee on Membership, the School Health Committee, and the Committee on Legislation of which he was chairman for many years. Dr. Darlington was a former director of the National Tuberculosis Association, former President of the Maine Thoracic Society, the Maine Lung Association and the Maine Society of Internal Medicine.

Dr. Darlington has served as Alternate Delegate to the AMA since 1974.

DR. MAXWELL, of Portland, was born there on February 16, 1939, son of Irving W. and Florence D. Maxwell. He was graduated from Middlebury College and received his medical degree from Boston University School of Medicine in 1966. He interned in Surgery at Boston University Medical Center from 1966 to 1967, served in the U.S. Army as a Captain from 1967 to 1969 and served a residency in Surgery and ENT from 1970 to 1973. He located in Portland in 1973 and is on the active staff at the Maine Medical Center and Mercy Hospital and on the consulting staff at the Bridgton Hospital.

He is a member of the Cumberland County Medical Association, Maine Medical Association, American Medical Association, National Legislative Communications Committee for the American Council of Otolaryngology, and President of Medical Mutual Insurance Co. of Maine.

Dr. Maxwell has been a member of the Executive Committee of the M.M.A. for the Second District since 1977, completing Dr. Douglas R. Hill's unexpired term.

DR. MAXWELL

DR. FEAGIN

DR. PHILLIPS

DR. FEAGIN, of Augusta, was born in Oxford, Mississippi on November 21, 1938, son of Oscar Rabb and Obion W. Feagin. He was graduated from the University of Mississippi, and received his medical degree from Johns Hopkins University School of Medicine in 1964. Dr. Feagin interned and served a residency at Vanderbilt University Hospital. In 1969, he located in Winthrop. He has been affiliated with the U.S. Public Health Service stationed in Augusta as Acting Director of Communicable Disease Control for the State of Maine and has practiced in Augusta since 1971. He is chairman of the Department of Medicine at the Augusta General Hospital.

He is a member and Secretary-Treasurer of the Kennebec County Medical Association, member of the Maine Medical Association, the American Medical Association, the American Society of Internal Medicine and the Maine Chapter of the American College of Physicians. He was a Fellow in Clinical Pharmacology in Nashville.

Dr. Feagin has been a member of the Executive Committee of the M.M.A. for the Fourth District since 1977, completing Dr. Richard T. Chamberlin's unexpired term.

DR. PHILLIPS, of Rumford, was born there on January 22, 1938, son of Kenneth M. and Margaret R. Phillips. He was graduated from Bates College and received his medical degree from Tufts University School of Medicine in 1964. Dr. Phillips served a rotating internship from 1964 to 1965, and a residency in General Surgery from 1967 to 1971 at the Maine Medical Center. He served in the U.S. Army Reserve as a Captain from 1964 to 1971. He has practiced in Rumford as a Family Practitioner from 1965 to 1967 and in General and Vascular Surgery from 1971 to the present, and is on the active staff and is Chief of the Department of Surgery at the Rumford Community Hospital and is on the courtesy staff at the Maine Medical Center.

Dr. Phillips is a member of the Oxford County Medical Society (and former Secretary), the Maine Medical Association, the Maine Vascular Society, the American College of Surgeons and is a Diplomate of the American Board of Surgery. He is also on the Executive Committee of the Maine Chapter, American College of Surgeons, and is on the Board of Directors of the Pine Tree Organization for Professional Standards Review, Inc. He has been a member of the Executive Committee of the M.M.A. for the Fifth District since 1976.

DR. GRIMES, of Lewiston, was born in Elizabeth, New Jersey, the son of Margaret M. and Edward G. Grimes. He was graduated from Bates College and received his medical degree from Hahnemann Medical College and Hospital, Philadelphia in 1958. He interned at the Central Maine General Hospital, served residencies there and at the Boston Floating Hospital, and took a postgraduate course at the Children's Hospital Medical Center in Boston. In 1962, he located in Lewiston where he is affiliated with the Central Maine Medical Center and St. Mary's General Hospital.

He is a member of the Androscoggin County Medical Society, the Maine Medical Association and the American Medical Association.

Dr. Grimes was appointed a member of the Executive Committee of the M.M.A. for the Seventh District in 1977 to serve until June 1978, when an election would be held to fill the vacancy left by Dr. Ross W. Green.

DR. GRIMES

DR. BOSTWICK

DR. HELFRICH, of Presque Isle, was born in Springfield, New Jersey on March 3, 1922, the son of Harry M. and Margaret P. Helfrich. He was graduated from St. Lawrence University and received his medical degree from Cornell University Medical College in 1950. He interned at the Brooklyn Methodist Hospital and served residencies there and at the University Hospital of Cleveland. In 1954, Dr. Helfrich located in Presque Isle.

He is a member of the Aroostook County Medical Society, and the Maine Medical Association and is a Delegate to the M.M.A. House of Delegates.

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SKILLED NURSING FACILITY PROGRAM

What is the Skilled Nursing Facility Program?

In some hospitals there may be a number of patients who do not need the intensive services which the hospital provides, yet are not well enough to go home. Some of these patients could receive the care they need in a Skilled Nursing Facility during recovery and release a needed bed for a more acutely ill patient.

In order to meet the needs of both these patients and their hospitals, Blue Cross and Blue Shield of Maine has developed a program to increase the use of Skilled Nursing Facilities by people of all ages, not just those eligible for Medicare.

At the present time, 13 of the 17 Medicare facilities are participating in the S.N.F. program. These are equipped to provide the range of services needed by patients who require medical supervision and skilled nursing care but are not likely to need the specialized services of a hospital, such as operating rooms, laboratories and X-ray departments.

What Does the Skilled Nursing Facility Program Do?

The program enables some hospital patients to be discharged sooner than usual to recuperate in a Skilled Nursing Facility and others to be referred directly to a S.N.F. without prior hospitalization. It cuts down the costs of medical care and helps relieve the shortage of hospital beds for the critically ill patients.

The Skilled Nursing Facility provides skilled nursing services, rehabilitation care and other services which the patient's physician may order, such as physical, occupational, speech and dietary therapy.

If the patient's condition should change, his physician may refer him back to a hospital.

Blue Cross and Blue Shield of Maine members will benefit by a reduction in the total cost of illness, since care in a S.N.F. is less expensive than care in a general hospital. This lower cost has the obvious effect of reducing Blue Cross and Blue Shield expenses, which helps to hold down subscription rates.

Who is Eligible?

All Blue Cross and Blue Shield of Maine members are eligible. Referral must be made by the patient's physician. The patient will receive the same Blue Cross and Blue Shield benefits in the Skilled Nursing Facility that he or she would receive in a hospital.

The patient will be provided with two days of care in a S.N.F. for each benefit day provided by the certificate. Example: If, at the time of admission, the patient had twenty-five benefit days available, Blue Cross would provide up to fifty days of care in a S.N.F.

What Does the Physician Do?

The physician determines whether the patient can be referred to the Skilled Nursing Facility Program and discusses the Program with the patient. He then reviews the plan of care with the participating Skilled Nursing Facility, which makes the arrangements for provision of care. The physician remains in complete charge of the patient and supervises the course of treatment provided.

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Hematogenous Osteomyelitis

A Report of Four Cases

MICHAEL A. LACOMBE, M.D., F.A.C.P. AND ROBERT B. FUNCH, M.D., F.A.C.R.

From the point of view of pathogenesis, osteomyelitis may be secondary to hematogenous spread of infection, to a contiguous focus of infection, or associated with peripheral vascular disease. Of these three modes of pathogenesis of osteomyelitis, that associated with contiguous infection is most common, whereas hematogenous osteomyelitis is the least frequent. In addition, hematogenous osteomyelitis has classically been described as a disease of children although some reviews have described a secondary rise in frequency in the older age groups.[1] We present here four cases of hematogenous osteomyelitis in adults with a discussion of the unusual sites of infection, the bacteriology of these cases, and the radiologic aspects of osteomyelitis in general.

CASE REPORTS

Case 1

Mr. A.G., a 32-year-old white male, was admitted because of pain, tenderness, and swelling in the area of the right sternoclavicular joint. He first noted pain and discomfort in that area some five weeks prior to his admission to the hospital, and at that time, he had an X-ray study done which was reported as normal. Because of continued pain and discomfort in the area, the patient subsequently came to the hospital, presenting with focal swelling, erythema, and exquisite tenderness in the area of the right sternoclavicular joint. His admission white blood cell count was 12,400. His admission sedimentation rate was 80 mm. per hour. Aspiration and culture of the right sternoclavicular joint yielded heavy growth of staphylococcal organisms, coagulase positive and penicillinase-producing. The patient was treated with Oxacillin 2 grams intravenously q4h for one month. His sedimentation rate on discharge was 8 mm. per hour, and his white blood cell count had returned to normal (See Fig. 1).

Fig. 1, Case #1. Osteomyelitis of proximal clavicle.

Case 2

Mrs. M.M., a 67-year-old woman, was admitted to the hospital because of pain in the left shoulder. The patient gave a history of chronic urinary tract infections, and in addition, had had repeated injections of corticosteriods in both shoulders because of presumed arthritis. At the time of her admission, an abscess in the left axilla was drained, and Proteus mirabilis sensitive to Keflin® and Penicillin was recovered. After three weeks of Cephalosporin - 2 gm. intravenously q6h, the patient developed an allergy to the antibiotic and was switched to Gentamicin - 60 mg. intravenously q8h for the last week of her hospital stay. Her admission white blood cell count was 15,300, and her sedimentation rate was 70. Her discharge sedimentation rate was 15 (See Fig. 2).

Fig. 2, Case #2. Osteomyelitis of humeral head.

Fig. 3, Case #3. Osteomyelitis of proximal tibia.

Case 3

Mrs. M.E., a 72-year-old lady, was admitted to the hospital because of recurrent pain, swelling, and tenderness in the left anterior tibial area. In 1940, following a two-year history of purulent drainage from the left anterior tibia, a diagnosis of osteomyelitis was first made. The patient had an osteotomy done at that time with protracted drainage of purulent material, and the osteotomy site healed spontaneously. Approximately ten years after that, the patient was again hospitalized because of discharge from the area of the osteotomy and was treated with a short course of antibiotics. Since that time, she has had chronic aching in the left anterior tibial area which had been construed as "arthritis." She had also given a history of periodic blackening of the skin around the area of the osteotomy site and said that occasionally, every 2-3 years, she would have a short period of drainage of pus from the area, each time being treated with oral Penicillin for 7-10 days with resolution of the drainage. Upon admission to Stephens Memorial Hospital at this time, radiographs of the area suggested the possibility of chronic osteomyelitis. Her admission sedimentation rate was 73 mm. An admission white count was 11,600 with a normal differential. The purulent drainage from the osteotomy site contained coagulase-positive staphylococcal aureus sensitive to Pencillin. Her blood cultures were negitive. The patient was begun on high dosages of intravenous Penicillin, 20 million units per day. Because of persistent pain and persistent discharge, the left upper tibia was explored surgically, and the entire infected area curetted. Pathological examination of the tissue showed chronic inflammation and granulation tissue with bony fragments showing osteomyetilis and subacute abscess formation. Cultures of the purulent material recovered at the time of surgery did not yield any organism. The patient was continued on 20 million units per day of Penicillin for one month from the time of surgery. Her sedimentation rate subsequently returned to normal at the time of discharge (See Fig. 3).

Case 4

Mr. C.L., a 57-year-old man was admitted to the hospital because of continued and protracted pain in the left foot. Radiographs disclosed marked destruction of the distal end of the first metatarsal. Blood cultures were positive for coagulase-positive staphylococcus aureus. On surgical debridement of the infected area, the same organism was cultured. He was treated with Oxacillin - 1 gram intravenously every 6 hours for a period of four weeks. Admission white cell count was 13,100 with 6% bands. His sedimentation rates were not obtained (See Fig. 4).

Of 62 cases of hematogenous osteomyelitis reported in an excellent review of osteomyelitis,[1] four involved the clavicle, eight the proximal humerus, twelve the tibia, and five the tarsal bones. As has been classically reported in the literature, staphylococcus aureus was the most common etiologic agent, as it was in three of our four cases. Although gram negative bacteremias have been reported with increasing frequency, osteomyelitis secondary to gram-negative organisms has remained distinctly uncommon. It was assumed that in Case 2, the Proteus osteomyelitis was secondary to hematogenous spread from her chronic urinary tract infections rather than secondary to repeated joint injection with corticosteriods. The clinical presentation of our four cases was variable but did not fit the classical description of hematogenous osteomyelitis presenting in children, that of sudden high fevers and

Fig. 4, Case #4. Osteomyelitis of distal first metatarsal.

toxic illness. Two of the four cases, Case 1 and Case 2, showed evidence of local suppuration about the involved bone, none had high fevers nor markedly elevated white cell counts, three of the four had markedly elevated sedimentation rates.

Osteomyelitis in its acute hematogenous form first produces multiple microabscesses in the marrow cavity. These can be anywhere along the length of the bone, but most often are at the end of the bone, usually involving metaphysis. This produces the earliest radiologic bone change of focal radiolucency or bone destruction. The epiphyseal plate is usually an effective barrier and prevents extension of the process into the epiphysis. If there is a joint effusion noted radiologically, it is usually a sympathetic effusion, although joint extension and involvement in general are more common in adults than in children. The exception to these generalizations on an adjacent joint involvement is tuberculosis of the bone where joint involvement is commonplace and usual. Deep soft tissue swelling is usually the earliest change demonstrated by radiologic examination, but unfortunately, this is nonspecific and can be seen in cellutitis in the absence of bone infection. Its importance, however, can not be over-emphasized, because it may be the only clue on radiographic examination early in the course of disease. The more specific and diagnostic destructive changes in the metaphysis are usually delayed at least 10 days after the onset of symptoms, so that early in the disease there are no diagnostic radiologic findings. At this stage, however, nuclear bone scanning will be positive, nonspecific as always, but will establish the diagnosis when interpreted in the context of the clinical picture, and will pinpoint precisely the anatomic site of involvement. The bone scan clearly distinguishes between cellulitis and osteomyelitis. As the disease progresses, the areas of osteitis and abscess enlarge and extend through the medullary cavity and can even involve the entire shaft if the disease is not modified by treatment. The extension of the infection through the cortex elevates the periosteum, stimulating the production of subperiosteal new bone. This will be seen on the x-ray film studies layered parallel to the shaft, but may take 3-6 weeks to be demonstrable. This cloak of new bone is called the involucrumen. On occasion, it is thick and not layered. It is never perpendicular to the shaft in the sunburst fashion that may be seen in malignant tumors, because the proteolytic enzymes of the pus destroy Sharpey's fibers. New bone may also form from the cortex and endosteum as the disease becomes more subacute or chronic.

The devascularized bone dies and sequestra forms in 3-6 weeks. These may discharge along with pus through cortical defects or cloacae, or may be absorbed if they are small. Small sequestra may not be visible radiographically because of surrounding sclerotic reaction. As healing takes place, the cavities fill in and fade on film study, and there is progressive sclerosis or eburnation. The subperiosteal new bone is assimilated with the cortex which thus becomes thickened.

The evolution of this full-blown course of the disease in the healing phase may be modified markedly by antibiotic therapy, and accordingly, the findings may vary greatly. If the disease is treated early and appropriately and vigorously, the x-ray findings may be very minimal with slight bone rarefacation or minimal subperiosteal new bone, or may even be absent. Osteoporosis should be apparent at the involved area because of disuse.

The combination of destructive and productive changes descrbed above is typical of ordinary bacterial pyogenic osteomyelitis. In tuberculosis, the changes are usually exclusively destructive in the absence of superimposed mixed infection and the changes in syphillis are usually purely productive. Thus, tuberculosis is the classical bone destroyer, syphillis the bone producer, and pyogenic osteomyelitis combines production and destruction.

In Case 1 the initial films of the right clavicle were normal, but studies three weeks later revealed multiple lucent defects which progressed over the next week (Fig 1) to partial destruction of the marrow cavity and inferior cortex of the proximal extremity of the bone (arrow). Plain film and tomographic studies showed some new bone formation two

months later.

In Case 2 typical early lytic and productive changes of acute osteomyelitis evolved to the appearance of the chronic phase in the proximal left humerous noted in Fig. 2. The head of the bone is 50% destroyed. The disease has involved the proximal 1/3 of the marrow cavity of the shaft with cloacal formation and involucrum. The shoulder joint has been involved and the healing phase had produced bony fusion or ankylosis at the glenohumeral articulation.

In Case 3 note the central cavity or lytic defect in the marrow space of the proximal left tibial shaft (Fig. 3, arrow). An old osteotomy surgical defect can be responsible for similar appearance, but increase in size of this lucency over four months establishes the presence of acute infection in the bone marrow. There is bony ankylosis of the knee joint.

In Case 4 focal destruction in the medial aspect of the left first metatarsal head has enlarged to the size noted in Fig. 4 (arrow). These preoperative x-ray films also reveal typical subperiosteal new bone or involucrum surrounding the distal metatarsal shaft. The entire bone is osteoporotic from disuse, and there is adjacent soft tissue swelling.

In summary, we present four cases of hematogenous osteomyelitis, the least common of the three pathogenetic forms of osteomyelitis. In three of the four cases, the offending organism was coagulase-positive staphylococcus aureus, and in the fourth case, Proteus mirabilis from gram-negitive bacteremia secondary to chronic urinary tract infection. In two of the four cases, the site of infection was distinctly unusual, i.e., the sternoclavicular joint and metatarsal head. In two of the four cases, surgical treatment was coupled with prolonged antibiotic therpy. In none of the four cases of hematogenous osteomyelitis presented here were the patients acutely and severely ill. All presented with pain, and three of four had markedly elevated sedimentation rates. All showed radiographic changes at the time of admission to the hospital.

It should be stressed that early in the disease there are no diagnostic radiologic findings. With a high index of suspicion, however, and in the context of the clinical picture, nuclear bone scanning will be positive albeit nonspecific and may establish the diagnosis so that treatment can be begun early. A bone scan will clearly distinguish between cellulitis and osteomyelitis and allow early treatment of serious infection.

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The Clinical Significance of Myocardial Rupture

A Review of 189 Cases of Acute Myocardial Infarction

WILLIAM L. MEDD, M.D., F.A.C.P.*

ABSTRACT

One hundred eighty-nine cases of acute myocardial infarction were reviewed over a period of three and a half years. The incidence of myocardial rupture was 3.7% of all cases admitted with a diagnosis of acute myocardial infarction. Myocardial rupture was the cause of death in 22.5% of all patients who died of acute myocardial infarction. The average age was 73.8 years. The average time between the onset of symptoms and rupture was eighteen hours. All but one patient presented with a prodrome characterized by agitation and increasing chest pain. The anterior wall was the most common site of rupture.

INTRODUCTION

Myocardial infarction causes death in several ways. A patient may die of cardiogenic shock, arrhythmia, electromechanical dissociation or rupture of the heart. With the advent of coronary care units, arrhythmias have become easier to treat and less frequently a cause of death. Cardiogenic shock remains difficult to treat, and myocardial rupture even more so, with most successful case reports being anecdotal. Electro-mechanical dissociation is most often untreatable and a terminal event.

Since mortality from infarction has decreased in general, myocardial rupture has become a more significant complication. Most series that are quoted in the literature[1-7] are reviews of autopsy data with retrospective chart reviews. Therefore, much of the information about myocardial rupture is not clinical. This review encompasses the experience with acute myocardial infarction and rupture of the heart at Stephens Memorial Hospital, Norway, Maine, from July 1974 through March 1978 (three and a half years). Through this review, a more accurate clinical picture of the role myocardial rupture plays in sudden death following acute myocardial infarction will be presented.

METHODS

One hundred and eighty-nine cases of acute myocardial infarction were reviewed. These included all cases of acute myocardial infarctions admitted to the CCU from July 1974 through March 1978. They were all cared for by the author or two internist colleagues. All data was collected by retrospective chart review, postmortem examination and direct involvement with every one of the patients.

TABLE 1

SUMMARY OF PATIENTS WHO SURVIVED ACUTE MYOCARDIAL INFARCTIONS AT STEPHENS MEMORIAL HOSPITAL FROM JULY 1974 THROUGH MARCH 1978

Total number of myocardial infarctions that survived	158 (84% of total)
Method of documentation of myocardial infarctions	
Enzymes alone (CPK plus MB isoenzymes)	32
EKG alone	9
Both	117
Age distribution	35 to 93 years
Average age	65.2 years

TABLE 2

AREA OF MYOCARDIAL INFARCTION IN PATIENTS WHO SURVIVED

Anteroseptal	47
Inferior myocardial infarction	44
Indeterminate (non-transmural)	30
Subendocardial	19
High lateral	6
Anterior lateral	2
Inferior lateral	4
Anterior	1
Inferior lateral, true posterior	2
True posterior	2
Inferior true posterior	1
Posterior lateral	2
Number of patients with more than one myocardial infarction:	
Two myocardial infarctions in the same patient	5
Three myocardial infarctions in the same patient	1
Four myocardial infarctions in the same patient	1

RESULTS

Table 1 reviews the characteristics of the patients who survived their acute myocardial infarction. One hundred and fifty-eight patients survived, with a survival rate of 84%. The age distribution was from 35 to 93, with the average age being 65.2 years. The ratio of male to female was approximately 1:1. The diagnosis was made by CPK isoenzymes (MB band) and/or electrocardiogram. One hundred and seventeen patients had elevated CPK isoenzymes and diagnostic electrocardiograms. Thirty-two patients

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TABLE 3

REVIEW OF PATIENTS WHO DIED OF MYOCARDIAL INFARCTION WHILE IN THE HOSPITAL

Number	31 (16% of total)
Age distribution	54-90 years
Average age	73.8 years
Sex distribution	18 females
	13 males
Number who underwent postmortem examination	16 (52% of total)
Cause of death:	
Shock alone	8 (25.8 % of total)
Arrhythmia	8 (25.8% of total)
Electro-mechanical dissociation	1 (3.2% of total)
Unknown cause of death	1 (3.2% of total)
Shock plus arrhythmia	6 (19.3% of total)
Rupture of the myocardium	7 (22.5% of total)
Types of arrhythmia causing death alone or in combination with shock:	
Ventricular tachycardia	1
Ventricular fibrillation	5
Asystole	12
Method of documentation of myocardial infarction:	
EKG plus enzymes plus CPK (MV enzymes)	16
EKG alone	11
Postmortem examination	4

TABLE 4

AREA OF MYOCARDIAL INFARCTIONS IN PATIENTS WHO DIED

Anteroseptal	18
Inferior	3
Inferior-posterior	2
Apical	2
Inferior-anterior lateral	1
Indeterminate	1
Inferior-lateral	1
Anterior septal-inferior-posterior	1
High Lateral	2

had elevated CPK isoenzymes only, and nine patients had diagnostic electrocardiograms only.

The area of myocardial infarction determined by electrocardiogram is presented in Table 2. The most common sites in descending order were: anteroseptal, inferior, nontransmural (elevated enzymes with nonspecific EKG changes) and subendocardial. In addition, five patients had two myocardial infarctions, one patient had three myocardial infarctions and one patient had four myocardial infarctions.

Table 3 summarizes comparable data in the thrity-one patients who died. They comprised sixteen percent of all acute myocardial infarctions admitted to the CCU. The age spread was 54 to 90 years, with an average of 73.8 years. There were eighteen females and thirteen males. Sixteen patients (52%) underwent postmortem examination. The diagnosis was made in sixteen patients by both electrocardiogram and CPK

Continued on Page 279

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TABLE 5

CLINICAL DATA ON THE PATIENTS WHO DIED OF MYOCARDIAL RUPTURE

Number of cases	7
Percent of all myocardial infarctions	3.7%
Percent of all deaths	22.5%
Age distribution	62-85 years
Average age	73 years
Sex distribution of rupture cases	5 female 2 male
Sex distribution of nonrupture cases	13 female 11 male
Length of time between onset of chest pain and rupture	6 hours to 26 hours and 45 minutes.
Average length of time	18 hours

Pertinent history prior to admission:

Case #1-	Myocardial infarction one year earlier with no symptoms in between.
Case #2 -	Three day history of indigestion and leading an active life during those three days.
Case #3 -	No prodrome
Case #4 -	Angina for two days prior to admission
Case #5 -	Four days of angina with an active life during those four days.
Case #6 -	One week of increasing angina and leading an active life during that week.
Case #7 -	No prodrome

History of hypertension:

Mild, on only diuretic therapy	3 out of 7 cases

Physical examinations:

Atrial gallop (on admission)	4 out of 7 cases
Systolic murmur	3 out of 7 cases
Shock prodrome	1 out of 7 cases

isoenzymes and in eleven patients by electrocardiogram alone. The cause of death was cardiogenic shock in eight patients, arrhythmia in eight patients, myocardial rupture in seven patients, shock plus arrhythmia in six patients, electro-mechanical dissociation in one patient and undetermined in one patient. The type of arrhythmia in descending order was: asystole, ventricular fibrillation and ventricular tachycardia. The location of the myocardial infarction is compiled in Table 4. The most common site was the anteroseptal wall with the other areas being evenly represented.

Myocardial rupture is obviously an important cause of death in this series. For this reason, the seven cases were reviewed to characterize the clinical entity more precisely. Table 5 reviews the clinical data for the group of seven patients. They comprised 3.7% of all patients admitted with acute myocardial infarction. Heart rupture occurred in 22.5% of all deaths due to myocardial infarction. The age spread was 62 to 85 years with the average age being 73 years. There were five females and two males, compared to thirteen females and eleven males in nonrupture deaths.

The length of time between the onset of pain and death ranged from 6 hours to 26 hours and 45 minutes, with the average time being eighteen hours.

TABLE 6

ENZYMES SUMMARY

CPK (total CPK/MB)	Normal Range - Total 5-80 IU/L MB 0-15 IU/L
Case #1	35/9
Case #2	56/14 day 1 114/22 day 2
Case #3	127 total day 1 1365 total day 2
Case #4	46/8
Case #5	75/15
Case #6	61/3 day 1 476/80 day 2
Case #7	290/57
SGOT	Normal range - 4-20 IU/L
Case #1	11
Case #2	2 day 1 52 day 2
Case #3	24
Case #4	not obtained
Case #5	21
Case #6	14 day 1 16 day 2
Case #7	49 day 1

TABLE 7

AREA OF MYOCARDIAL INFARCTION

	EKG	*Area of rupture by postmortem*
Case #1	Anterior wall and apex	Anterior wall
Case #2	Anterior wall	Posterior wall
Case #3	Inferior posterior lateral	?
Case #4	Anteroseptal myocardial infarction	Anterior wall
Case #5	Panapical	Apex
Case #6	Anterior myocardial infarction	Anterior wall
Case #7	Anteroseptal myocardial infarction	Anterior wall

Coronary circulation:

Case #1	Not possible to tell
Case #2	Right coronary occluded; left coronary patent
Case #3	Right coronary occluded; circumflex occluded
Case #4	Left anterior descending; circumflex occluded
Case #5	Three vessels occluded
Case #6	Left main only
Case #7	Left anterior descending occluded

Pertinent historical data prior to admission for each patient are presented. Three patients had no prodrome (one of these had had a myocardial infarction one year prior to death) and four had a two-to-seven-day history of angina prior to the myocardial infarction with all leading an active existence during this period of time. The physical examination prior to rupture revealed that four patients had an atrial gallop, three patients had systolic murmurs and one patient was in cardiogenic shock. Three out of seven patients had mild hypertension treated by diuretics alone.

The area of rupture and the coronary circulation is

Table 8

Management Data

Medication administered:

Case #1	Nipride® briefly, Lidocaine continiously per PVC's (patient was on Lidocaine during rupture)
Case #2	Dopamine briefly for hypotension, Lidocaine for PVC's (on at rupture)
Case #3	Levophed briefly; patient was put on Digoxin, Lasix® and Quinidine (was on these at rupture)
Case #4	No medication
Case #5	No medication
Case #6	Nitroprusside briefly; no other medications
Case #7	No medication

Swan-Ganz catheter:

Two cases had the Swan-Ganz catheter in. The wedges just before rupture were 11 in one case and 8 in the other.

Pacemaker:

Two cases had a pacemaker.

reviewed in Table 8. Six of the seven cases showed anterior wall injury on electrocardiogram, and one showed an extensive inferior-posterior-lateral injury pattern. At postmortem the rupture occurred in the anterior wall in four cases, the apex in one case, the posterior wall in one case and an indeterminate area in another. The coronary circulation data revealed: two patients with one-vessel disease (one of them had a right coronary thrombosis); two patients had two-vessel disease; one patient had a left main lesion; one patient had three-vessel disease. In one case, the coronary anatomy was not presented well enough to decide on the significant coronary lesion.

Pertinent management data is presented in Table 8. Two patients had significant hypertension initially, requiring nitroprusside for a brief time. They did not become hypertensive again. Two patients had hypertension requiring norepinephrine or dopamine for a short period. Only one patient was on a digitalis preparation. Two patients were on lidocaine for PVC's at the time of rupture. A Swan-Ganz catheter was used in two cases. The pulmonary wedge pressure just prior to death was 11 and 8 respectively. Two cases had a pacemaker in place at the time of rupture.

In this series the prodrome prior to rupture has been similar for all seven cases (Table 9). One case died suddenly without symptoms. Another case had intermittent mild pain and died suddenly. The other five cases were either very uncomfortable and agitated or had increasingly severe pain. All seven died with sudden electro-mechanical dissociation.

Discussion

This series of myocardial rupture cases adds new data to the existing concepts about rupture of the heart as a cause of death in acute myocardial infarction. The incidence of myocardial rupture as a cause of death is generally considered to be 10%.[1,7,8] The incidence in this series is 22.5% of all deaths due to

Table 9

Myocardial rupture prodrome

Uncomfortable and agitated; sudden death with electro-mechanical dissociation	2 cases
Stable with sudden death and electro-mechanical dissociation	1 case
Sudden severe pain with electro-mechanical dissociation	1 case
Stable followed by increasing pain with electro-mechanical dissociation	2 cases
Intermittent pain with sudden onset of electro-mechanical dissociation	1 case

acute myocardial infarction, suggesting that rupture may occur more frequently than generally accepted in the literature.

It is state that "Rupture on the first day suggests the infarction occured a few days earilier"[8] Several other articles[1-4,6,7] refer to this time sequence between the onset of the myocardial infarction and rupture. In summarizing these articles, the general consensus is that 25% rupture the first day, 50% by the third day and 70% by the fifth or sixth day. In this study the average length of time from onset of pain to rupture was eighteen hours, with the shortest being 6 hours and the longest about 27 hours.

Age is an important factor. The patients who survived their infarction were younger (average 65.2 years), compared to those who died of all causes (average 73.8 years). Patients who ruptured were about the same age (average 73 years) as the other patients who died. This is in agreement with the literature in terms of rupture being an event in the elderly.[2,7] There were a greater number of female patients (5:2). The patients who died of other causes were about equally distributed between males and females. Two authors found the ratio of male to female almost equal.[1,7] One author[5] felt it was more common in females. Our data support this view, especially when it is compared to the patients who died of other causes. The data on CPK/MB fraction isoenzymes was not very helpful. They were all obtained on admission to the hospital, but most patients died before second samples were drawn. One would conjecture that the values would be higher, but only one case had a high value in the second sample of blood.

The location of the rupture in one series[7] was distributed in the following manner: 35% - anterior wall, 35% - posterior wall, 20% - lateral all, 10% - apex. The postmortem examinations in this series revealed four anterior wall ruptures, one posterior wall and one apical rupture. The major difference appears to be in the lower incidence of posterior wall rupture.

The number of coronary vessels involved with atherosclerosis does not appear to be an important factor. The intensity of the necrosis and size of infarct are important from our postmortem data. This has been found in other series to be important.[9]

Severe, extensive, previous myocardial disease is not a prerequisite.[7] In the seven cases in this report, only one patient had a previous myocardial infarction. The postmortem data did not reveal extensive old fibrosis.

Pertinent information with regard to prodromal symptoms has emerged from this review. Five of the seven cases had a two-to-five-day prodrome of increasing angina. All of these patients were quite active prior to hospitalization. This further emphasizes the perennial problem of getting the patient to the hospital at the earliest sign of coronary perfusion instability. Once these patients reached the hospital, they were put at bedrest so that activity during the actual process of the acute myocardial infarction did not play a role in coronary rupture. This factor has been advocated as a pertinent risk for myocardial rupture by a previous article[1] Pre-existing hypertension has been labelled as a risk factor for rupture.[1,8] Only three patients had pre-existing hypertension which was mild and well-controlled.

Hypertension during the myocardial infarction has been included as a risk factor for rupture.[1,7,8,9] Only two patients had hypertension on admission. Both were quickly controlled with nitroprusside, which was subsequently stopped. None of the patients were hypertensive within six hours of rupture. Therapy prior to rupture has been addressed, and there is little support for digitalis or anticoagulants playing any role in the etiology of rupture.[2] No pattern can be seen in therapy in this series of seven either. Several interesting findings need to be brought out. Only four patients had atrial gallops. Two of the patients had Swan-Ganz catheters in place, and just before rupture the pulmonary wedge pressure was normal. This further emphasizes the intense necrosis with good function of the remaining myocardium.

In two reports, it has been stated that the prodrome of rupture appeared to be benign, and most patients died suddenly without premonitory symptoms.[7,8] This was not the case in this series. Only one patient died with no prodrome. All other patients either were agitated, uncomfortable or had increasing chest pain.

Although patients have survived myocardial rupture with surgical intervention,[8] it still remains nearly an impossible complication to treat. Most patients who have myocardial infarctions are not at cardiac surgery centers. In addition, there is virtually no time to wait so that the survival hinges frequently on the fortuitous fact that a patient might be in surgery, having cardiac catheterization or already on a counter pulsation pump. A rare case has survived because of tamponade from the preicardium and the ability to maintain some cardiac output for a period of time. It would appear that if the 3.7% incidence of death from rupture in all myocardial infarctions is to be reduced, we must preserve the heart muscle and prevent extensive transmural damage. The type of therapy to preserve the ischemic myocardium can be carried out in small and large hospitals[10] Judicious use of the Swan-Ganz catheter to monitor cardiac output and left ventricular end-diastolic pressure allows one to use long-acting nitrates, beta blockers and blood pressure lowering in the acute myocardial infarction. When indicated, these medications may decrease the intensity of myocardial necrosis. Although hypertension itself is not a risk factor in this group of patients, it would appear logical that hypertension would increase the work on the heart and increase the risk of rupture in certain cases.

The major deficiency in this study is the 52% postmortem rate. It would have been more accurate to have obtained a postmortem on all deaths. Despite this deficiency, I feel the patients who died without postmortem were easily characterized and did not fit the emerging pattern of the seven cases who had myocardial rupture. Possibly the incidence of rupture might be higher had postmortem examinations been obtained on all patients. The historical and clinical data might be altered if one or two cases were missed due to the absence of a postmortem exam.

Conclusion

One hundred and eighty-nine acute myocardial infarctions have been reviewed with specific attention paid to the incidence and characteristics of the patients who died of myocardial rupture. The incidence of rupture as a cause of death was higher than that stated in the literature. The age distribution was similar. The area of rupture was almost exclusively the anterior wall. Pre-existing hypertension and hypertension just before death did not play a role in rupture. Unstable angina pectoris was an important historical factor in this case summary. Prerupture therapy did not influence the development of myocardial rupture, and the patients (except for one) were experiencing their first myocardial infarction. If a patient is uncomfortable, agitated, having persistent pain or increasing pain, then they are at high risk for myocardial rupture and usually this will occur within the first twenty-four hours.

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Skinny Needle Cholangiography in The Differential Diagnosis and Management of Jaundice

ROBERT B. FUNCH, M.D.

The introduction of the Chiba thin needle has increased the safety and reliability of percutaneous transhepatic cholangiography and has sparked renewed interest and use of this technique in the study of the jaundiced patient.[14] This skinny needle technique for the visualization of the biliary ductal system is now an established procedure in the diagnosis and management of hepatobiliary diseases.[3,4,11] Among its particular advantages are the relative simplicity and speed of performance, high success rate, lack of serious complications, and ready availability even in the smallest community hospital, since the easily learned technique requires no sophisticated equipment or training. This report will include experience with nine consecutive cases from August 1977 to May 1978 in a fifty-bed, acute care, general community hospital.

Indications.

The principal role of skinny needle cholangiography is to establish the presence or absence of obstruction of the biliary ductal system in the patient with a presumed or uncertain cinical and laboratory diagnosis of cholestatic jaundice.[10] This question is answered reliably and the question of the level of the obstruction is usually answered equally well. The nature of the obstructive lesion is the most difficult question to answer and the distinction between stone, tumor, stricture, and extrinsic compressing mass may be uncertain.

The probability of successful duct opacification by intravenous cholangiography (I.V.C.) diminishes rapidly with total serum bilirubin levels over 3 mg. per 100 ml. and I.V.C. is frequently not helpful even when combined with conventional tomography. Computed tomography and gray scale B mode ultrasonography are commonly used, non-invasive studies when available but never exclude surgical jaundice, because stones, stricture, etc. may commonly be present without proximal ductal ectasia.[7] The demonstration of normally sized intra- hepatic bile ducts by these two techniques is, therefore, not conclusive in differentiating medical from surgical jaundice. Conversely when computed tomography and ultrasonography demonstrate dilated ducts the direct opacification of the biliary tree by cholangiography may still be indicated to demonstrate the precise level and nature of the obstruction prior to surgery. Knowledge of such anatomic detail can obviate unnecessarily difficult surgical exploration and can save precious time at operation with possible reduction in surgical morbidity and mortality. The determination of the site and extent of a stricture is essential for proper surgical management. For bile duct cancers, those in the distal duct may be resected and bypassing more proximal tumors may lead to remission of jaundice and prolong life. On the other hand, inappropriate surgery may not relieve jaundice and may hasten death. Thus, the mere knowledge of obstruction alone is not enough. The more precise anatomic information the surgeon has preoperatively the faster, safer, and more effective the surgical treatment can be and when no obstruction is demonstrated the cholangiogram justifies delay or avoidance of surgery and its attendant increased morbidity in jaundiced patients with parenchymal liver disease.

Transhepatic percutaneous cholangiography (T.P.C.) may be more readily available than endoscopic retrograde cholangiopancreatography (E.R.C.P.) at smaller institutions where endoscopic capabilities may be lacking. It is probably quicker, less expensive, safer, and certainly has a higher success rate. It can be performed in patients when prior biliary-enteric surgical anastomosis precludes E.R.C.P. In many institutions T.P.C. has replaced E.R.C.P. as the procedure of first choice. The latter technique, however, has obvious superiority in demonstrating problems other than jaundice such as pancreatic disease, gastric and duodenal mucosal lesions, peptic ulcer and tumor. The preference for the initial use of T.P.C. is not completely universal but at least one group preferring E.R.C.P. compare it with a conventional 18 or 20 gauge needle and complication rate of 10 to 12% rather than with the 23 gauge thin wall needle which has now largely replaced the conventional sheathed needle.[5]

Contraindications.

Contraindications are few and include uncontrollable coagulation defects or bleeding diathesis and contrast agent sensitivity. The presence of a known vascular lesion of the liver and ecchinococcal liver disease are contraindications to liver puncture and the area of puncture may have to be changed if there is suppuration in the proposed site.

Technique.

Satisfactory bleeding parameters should be con-

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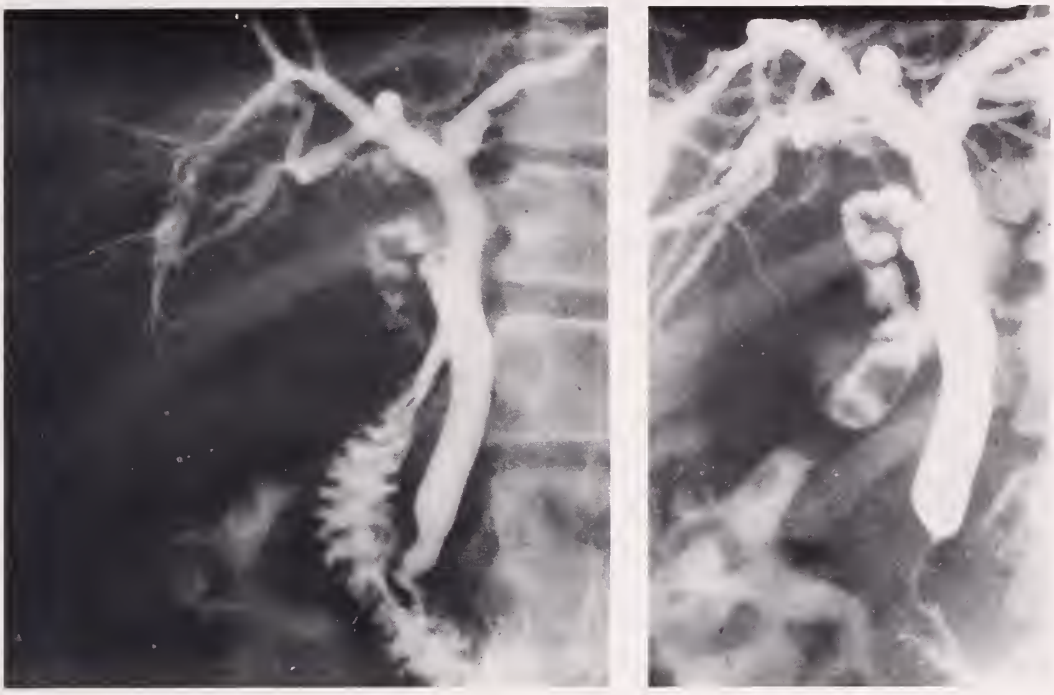

Fig. 1(a). Complete filling of the hepatic and common bile ducts obtained by T.P.C. with the needle tip in a very small peripheral right hepatic bile duct. No obstruction. Good duodenal filling. (b). Cystic duct and gallbladder containing calculi visualized only on delayed filming.

firmed beforehand and prophylactic antibiotics are recommended if the patient is icteric or there is a history of cholangitis. Up to 50% of cases with common duct obstruction have bacterial colonization and the pressure in the obstructed ducts may exceed that in the venous system, creating bile-blood fistulae along the needle tract and significant bacterial contamination of the systemic circulation.[2] Biliary sepsis is not an absolute contraindication to T.P.C. but in these patients care must be taken to avoid overdistension of the injected ducts. If an obstruction is found, immediate laparotomy is not mandatory but antibiotics must be continued while awaiting surgery.

The lateral approach we have used is probably the most popular and provides a longer needle tract through the liver substance for tamponade of subsequent bleeding or bile leakage from the interior of the liver. After sterile preparation of the puncture site and 1% Xylocaine® local anesthesia, the O.D. 0.7 mm. thin wall, 23 gauge needle and stylet are introduced in a single, rapid thrust during a brief period of end respiratory apnea. The eighth or ninth intercostal space in the right mid-axillary line is selected as the puncture site on the basis of clinical and fluoroscopic evaluation of liver size and configuration, and the needle is directed 30 degrees cephalad and in a plane horizontal to the table top. The needle is placed slightly above the confluence of the main intra-hepatic ducts and the needle tip deposited just to the right of the T-11 or T-12 vertebral body. The stylet is withdrawn and as shallow or normal breathing is resumed, the needle will bend or wave cephalically and caudally quite visibly with the excursions of the diaphragm. It is this very extreme flexibility of the skinny needle that largely prevents tearing of the liver and its vessels and the 30 degree non-cutting bevel reduces the likelihood of bleeding.

Identification of the position of the needle tip is accomplished by the injection-withdrawal technique. One-two ml. of 30-50% methylglucamine diatrizoate are injected while the needle is slowly withdrawn and fluoroscopic recognition of the site of contrast deposition is easily learned. If the needle tip is in the hepatic parenchyma, the contrast appears as an amorphous blob and persists. In the hepatic venous channels, it flows at once and rapidly toward the right atrium and has the appearance of the usual vascular channel or stellate network of channels. In the bile ducts, the contrast flows more slowly in a hepatofugal fashion and persists for a long period being easily recognized as bile duct. Continued injection of small increments is made until the entire duct system is filled and the duodenum identified or a point of obstruction is noted. (Fig. 1). We place strong reliance on fluoroscopic spot films, and overhead and tomographic films are exposed as needed in AP and oblique projections. Cross-table lateral may be helpful in selected cases but the patient should not be rolled on the side for overhead lateral film until the needle has been removed. Semi-erect, erect, and prone films are possible after the needle is withdrawn if the patient is able to rotate or stand.

Aspiration of viscid bile through the narrow needle is usually not successful from a small peripheral duct, often prolongs the procedure, and is not necessary for safety if over-filling of the ducts is avoided.[8] If bile can be removed from a central, larger duct, it is

replaced volume for volume by contrast using the least volume necessary in order to minimize complications.

If a bile duct has not been successfully entered on repeated injection and full withdrawal of the needle, subsequent passes are made altering the direction of the needle through a series of ten degree, fan-like steps superiorly and inferiorly and dorsally and ventrally until a duct is finally entered. The practical application of this technique of duct puncture is technically simple and easily learned without extensive training or experience.

Success rate and complication rate.

The rate of successful opacification of the biliary ducts approaches 100% with those who put no limit on the number of repeated passes permitted. Ferrucci and Wittenberg report 94% overall success in 100 cases with 99% success when the ducts were dilated and 82% success with normal caliber ducts.[3] Okuda reports 100% success in 95 patients with dilated ducts and 67% in 134 patients without obstruction.[14] Our own experience is that of success in all of our nine consecutive attempts.

Possible complications in addition to hemorrhage or bile peritonitis include cholangitis, gram negative septicemia, and a pneumothorax. With previous techniques, the incidence of bile leakage and peritonitis and hemorrhage has been up to 25%. With the skinny needle, Okuda reports a complication rate of 7.9% in 314 cases including a 3.5% incidence of bacteremia and with increasing experience the complication rate continues to decrease.[14] Ferrucci reports two cases of pneumothorax in 100 cases and sepsis in four patients with dilated ducts in a series of 100 patients and low grade febrile rections within two to three hours in seven of 100 patients with dilated ducts.[4] Flemming, et al report a single complication of gram negative septicemia in 88 patients.[1]

Problems in interpretation.

If T.P.C. is not successful, the probability of parenchymal disease strongly outweighs the probability of obstruction since dilated ducts are entered more easily than normal ducts.[1,5,15] However, obstruction is not excluded and the presumptive diagnosis of non-surgical jaundice is not justified or absolute. Ritchie, for example, found extra-hepatic obstruction in 50% of 14 failures.[13] We have had cases positive for obstruction in whom we would not have visualized the ducts if we had not persisted and used multiple passes. If we had quit after five or six passes, we would have falsely considered this indirect evidence of non-dilated ducts. Others have emphasized the same point to justify the use of multiple passes and persistent attempts to cannulize the ductal system.[4,13] Those who put no limit on the number of passes report rates approaching 100% in both dilated and normal ducts. Therefore, under no circum-

Continued on Page 286

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CONTRAINDICATIONS Hypersensitivity to oxycodone, aspirin, phenacetin or caffeine.

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Usage in children PERCODAN® should not be administered to children.

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PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

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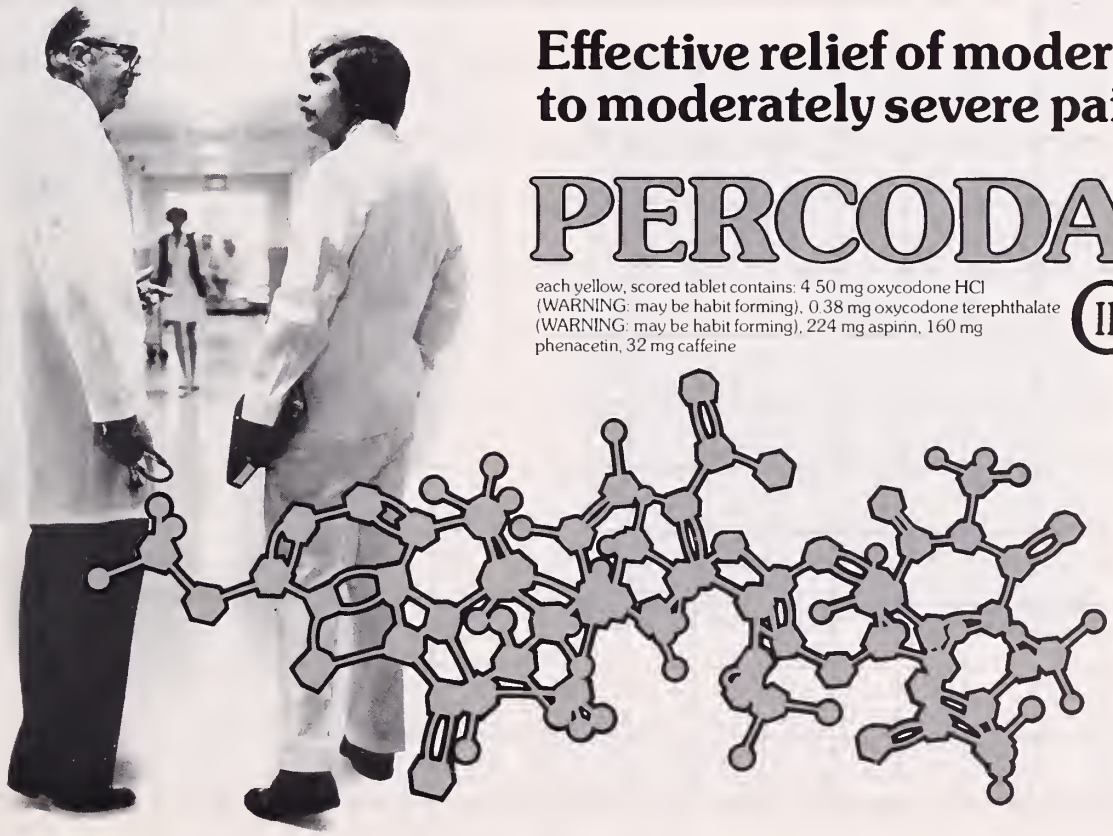

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Fig. 2. Typical appearance of a network of beaded serpiginous lymphatics to left of common hepatic duct and extending toward porta hepatis. Cystic duct obstructed in patient with acute cholecystitis.

Fig. 3a

stances, is it appropriate to presume any information if the biliary system is not entered and visualized successfully. Such failure should be considered technical and no presumption is drawn if false diagnoses are to be avoided.

Fig. 3b

Fig. 3c

Fig. 3(a). Early film showing dilated hepatic ducts. Hazy interface of contrast and stagnant dense bile simulates the point of obstruction. (b). Delayed film after continued injection shows sharp margin of solid obstruction at distal common bile duct due to pancreatitis. (c). Hypotonic duodenogram with barium reflux into distal common bile duct outlining lower limit of the short stricture which simulates malignant stricture.

The slow flow of the contrast test doses in the adventitial compartments permits easy differentiation from contrast in the lumen of the biliary system where centrifugal flow is more rapid. The filling of lymphatics is better appreciated in the film record than at fluoroscopy (Fig. 2). These vessels are beaded and serpiginous and rarely over two-three mm. in diameter, extending singly or in a network inferiorly and medially to the porta hepatis.

Location of the precise level of an incomplete obstruction is easy and accurate. There is a serious potential for error, however, when the obstruction is

Fig. 4. Marked dilatation proximal ductal system, abrupt stricture margin with downward convexity typical of malignant stricture. Tumor nodule seen as filling defect in the distal common duct in a 94-year-old male with invasion of the cystic and common bile ducts by adenocarcinoma of the gallbladder.

Fig. 5. Short stricture with abrupt margin and marked proximal ductal dilatation in 78-year-old woman with invasion of common bile duct by adenocarcinoma of the gallbladder.

of high degree or complete.[8] With poor distal flow and increased viscosity of the stagnant bile proximal to the lesion, there can be incomplete mixing of the contrast and the dense bile column. These admixture pseudo-defects can lead to a false diagnosis of a more proximal location of the level of the obstruction. This can result in failure to detect distal common duct stone or in a diagnosis of a high peri-portal obstruction when in reality there is a localized distal peri-ampullary lesion. A hazy, poorly defined interface between the contrast and the bile should suggest this incomplete mixing of the two, in contrast to the sharp definition which should be obtained against a solid obstruction (Fig. 3a). We have found delayed filming with prolonged injection time but without over-distension and the use of prone and erect filming after removal of the needle permit the contrast material to filter through the dense inspissated bile to the true site of the block (Fig. 3b). This same procedure and delayed studies are necessary if the cystic duct and the gallbladder are also to be identified (Fig. 1a and b).

Possible etiologies to be considered once the obstructing lesion has been identified can be grouped as stone, stricture, or tumor. These would include calculus, sclerosing cholangitis (multi-focal sclerosing fibrosis), post surgical stricture, pancreatitis, cholangitic carcinoma, carcinoma of the gallbladder, carcinoma of the pancreas, and metastasis from the gallbladder, pancreas, or adenocarcinoma of the liver.

Interpretation can be uncertain for several reasons. Tumor, for instance, will typically present with a convex downward meniscus but can mimic the downward concave contrast margin expected in stone (Fig. 4, 5). It can even present as a diffuse stricture or multiple short strictures when present as a sclerosing carcinoma and, thus, simulate cholangitis. A malignant obstruction in general is more likely to have greater dilatation than a benign stricture. Common bile duct cancers are usually short, well demarcated, or associated with irregular polypoid masses in the lumen. We have seen the same appearance with invasion of the common duct by carcinoma of the gallbladder (Fig. 4, 5). Tumor should probably be considered in the differential diagnosis of all cases of obstructive jaundice with stenosis or occlusion of the ducts.[1,9] A smooth taper in the intra-pancreatic portion of the common duct is expected in pancreatitis. The peri-hilar metastases and lymph nodes tend to appear as extrinsic compressions. The pseudo-calculous defect described by Meyhed and Evans presents no problem in diagnosis when the patient is fluoroscoped to identify the cyclic nature of the defect and the lack of obstruction to duodenal filling.[12]

If G.I. series is to be done, we prefer to perform it after the T.P.C. so that residual barium will not interfere with visualization of the biliary apparatus. We have followed the cholangiogram immediately by G.I. series and hypotonic duodenography while the obstructed ducts remained opacified (Fig. 3c). This afforded an excellent demonstration of the relation-

Fig. 6(a). Large gallbladder filled by T.P.C. via patent cystic duct. Multiple non-opaque calculi present. (b). Enlargement of distal common duct showing linear filling defect of calculus.

TABLE 1

DIAGNOSES OF THE NINE JAUNDICED PATIENTS UNDERGOING T.P.C. AT STEPHENS MEMORIAL HOSPITAL

Carcinoma of the gallbladder	2
Cholangitic carcinoma	1
Pancreatitis	1
Surgical stricture and fistula	1
Choledocholithiasis	2
Cholecystitis or cholelithiasis without common bile duct obstruction	2

ship of the lesion to the duodenum and ampullary area. Because of reflux of barium through the sphincter into the distal common bile duct, both sides of the obstructing lesion could be seen and the length and precise location of the stricture were clearly demonstrated for the surgeon.

Stephens Memorial Hospital experience.

The nine patients studied at Stephens Memorial Hospital ranged in age from 33 to 94 years with a median age of 76. There were five male patients and four females. All presented with the clinical picture of obstructive jaundice and were examined with the technique described above (Table 1). There were no failures to cannulate the duct system. In three patients only a single needle pass was necessary and the largest number of passes was eight, with an average of three. Four of the patients also had G.I. series but the T.P.C. was the diagnostic procedure of first choice once a diagnosis of cholestatic jaundice was made.

The two patients with malignant stricture due to adenocarcinoma of the gallbladder had marked proximal ductal dilatation and a high degree of obstruction of the common bile duct (Fig. 4, 5). The obstruction site showed a sharp but convex downward meniscus and one exhibited a tumor nodule in the distal duct (Fig. 4). The other revealed a single gallbladder stone. The patient with cholangitic carcinoma also had marked proximal ductal ectasia and showed complete obstruction of the common bile duct with a similar meniscus. Successful palliative intestinal-biliary bypass procedures were possible in all three patients and greatly facilitated by the anatomic detail revealed to the surgeon by the biliary opacification procedure.

The cholangiographic findings in the patient with pancreatitis were essentially the same as in these three malignancies and we, in fact, made a false diagnosis of malignancy on this basis early in our experience (Fig. 3). We are now more aware of the difficulty in identifying the nature of the obstructing lesion unless there is an obvious or unmistakable faceted or laminated stone.

Benign lesions can appear malignant as in this case and others have reported malignant lesions appearing benign as in multi-focal cholangio-carcinoma simulating sclerosing cholangitis.

Identification of a postoperative stricture in a jaundiced male who had sustained a known common duct injury at prior surgery was not difficult but an associated fistula to the duodenum was not appreciated.

The two patients with common bile duct and hepatic duct stones were easily diagnosed and appropriately treated surgically (Fig. 6).

In the remaining two patients, patency of the common bile duct was clearly established (Fig. 1,2) and

the cholecystectomies for cholecystitis in one and cholelithiasis in the other could be safely postponed. Inappropriate emergency surgery could be safely avoided as the jaundice subsided and the patients were conservatively prepared for elective treatment some days later.

There were no known instances of hemorrhage or bile leakage. Transient fever was the only complication. Some patients experienced mild or moderate discomfort in the right upper quadrant during the procedure but more complaints concerned the length of time on the hard fluoroscopic table.

Conclusions

1. Percutaneous transhepatic cholangiography is not a new technique and is one-half century old. The availability of image amplification fluoroscopy has increased its ease of performance and the introduction of the skinny needle by Okuda has made it a very safe procedure.

2. It is probably the most useful potential source of practical information if laparotomy is necessary to correct biliary obstruction and the single examination capable of preventing unnecessary exploration of the jaundiced patient with primary liver parenchymal disease.

3. The technique does not require extensive training and was easily learned and performed in a small community hospital with standard fluoroscopic and radiographic equipment. It is easily and quickly performed, relatively inexpensive, strikingly reliable, and relatively safe.

4. The presence or absence of obstruction and localization of the lesion are reliably demonstrated but determination of the nature of the lesion is not always certain.

5. No significance may be reliably attached to the failure to cannulate a duct.

6. The importance of delayed filming to prevent errors because of failure of mixing of the contrast and stagnant viscid bile is stressed.

7. Tumor must be included in the differential diagnosis in all cases with stenosis or occlusion of the bile ducts. Benign lesions may simulate malignancy and vice versa.

8. Skinny needle percutaneous transhepatic cholangiography has rapidly become an established and highly valuable tool in the diagnosis and management of the jaundiced patient.

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Fall Meeting of the M.M.A. House of Delegates

Saturday, December 9, 1978

Mid-Maine Medical Center (Thayer Unit), Waterville, Maine

12:30 P.M.—Registration; 1:00 P.M.—Lunch; 2:00 P.M.—Meeting

10:00 A.M.—Meeting of the Executive Committee

Primary Pneumococcal Peritonitis in an Adult

H.S. Sodhi, M.D., F.R.C. Path., F.A.C.P. *

Introduction

Primary peritonitis has been defined as a peritoneal inflammation that does not originate within the peritoneal cavity, but arises from an outside focus of infection.[1,2,3] Primary peritonitis occurs mainly in infancy and childhood, but cases have been reported at all ages.[1] Prior to advent of antibiotics, primary pneumococcal peritonitis was noted in two percent of pediatric emergencies, but now very few cases have been reported.[2] Primary pneumococcal peritonitis in adults is rare and between 1945 and 1970 only 50 cases have been reported in literature.[2]

I wish to report a case of primary pneumococcal peritonitis and review the literature on this condition.

Case Report

The patient, a 42-year-old white female was admitted to the hospital with the chief complaint of severe abdominal pain which was generalized throughout the abdomen; vaginal bleeding; fever and malaise. Since the last 4 days, patient had become weaker and abdominal pain had become more severe. Patient also developed diarrhea, cramping pain and black stools.

Past history revealed that patient delivered a viable male infant two months earlier. In the postpartum period, patient developed urinary tract infection with E. coli which was adequately treated with Ampicillin. Patient had usual childhood infections such as measles, mumps, chicken pox and pertussis.

Physical examination on admisssion revealed an anxious 42-year-old female, with weight of 92 lbs.; BP 120/80 mm of Hg.; pulse rate per minute and temperature of 100°F. Respiratory rate of 24 per minute. Lungs were clear on both sides. Abdominal examination revealed moderate degree of pain and tenderness on deep palpation in the pelvic area. Bowel sounds were present. Vaginal examination was painful and showed retroflexed and fixed uterus. Bleeding was noted from the cervix. Abdomen had diffuse guarding and rebound tenderness. Tenderness was most marked in the left lower quadrant. Uterus was retroflexed with marked tenderness on touch of the cervix.

Laboratory examination revealed the hemoglobin to be 12.5 g/dl; hematocrit 39%; white blood cell count 28,200/mm with neutrophils 94%; lymphocytes 5%; monoctyes 1%. Urine showed specific gravity of 1.019; albumin and sugar negative; 100 white blood cells per high power field. Cultures from blood, vaginal swab, stool, and throat swab showed cultures of Diplococcus pneumoniae. Blood examination showed total protein 6.1 Gm/dl; albumin 3.1 Gm/dl; sodium 131 mEq/1; potassium 3.1 mEq/1; chlorides 81 mEq/1; and CO_2 18 mEq/1.

Chest x-ray showed no abnormality. Plain x-ray of abdomen showed a small bowel gas pattern suggestive of adynamic ileus.

The patient was admitted to the hospital and treated with Tetracycline, Cleocin® and Gentamycin. After 48 hours, her temperature dropped and vital signs became stable. Although the culture indicated a sensitivity to Keflen®, it was not administered because the patient had given history of pencillin allergy.

Five days after admisssion, pelvic examination revealed a mass behind the retroflexed uterus. The uterus was fixed to this mass. On laparotomy, a large abscess behind the retroflexed uterus was noted. This was drained through posterior fornix. Culture obtained at surgery from the abscess was sterile. Both fallopian tubes were adherent to the abscess wall and were resected and both fallopian tubes showed acute inflammatory changes. Postoperatively, the patient developed severe hemorrhage through the drainage wound in the posterior fornix. Pouch of Douglas had necrotic tissue and a hysterectomy was performed. Patient had an unremarkable recovery. Pneumococcus was isolated from three blood cultures, vaginal exudate, throat culture and stool at time of admission. After antibiotic therapy, cultures from the pelvic abscess were sterile.

Discussion

Primary pneumococcal peritonitis constitutes not more than 1-2% of infancy and childhood infections. It has been reported at all ages, but infection in adults is very rare. Four avenues of invasion of peritoneal cavity have been described (i.e., the genital tract, transdiaphragmatic-lymphatic, gastrointestinal tract and the blood stream.[1,2] Specimens for culture of blood, throat, stool and vaginal exudate were positive; thus the route of spread of infection in this case is a matter of conjecture.

The association between nephrotic syndrome, juvenile cirrhosis with ascites,[1] chronic alcoholism with Laennec's cirrhosis,[4] and postnecrotic cirrhosis[5] have been reported in literature. In our case, no evidence of cirrhosis or nephrosis was noted.

No definite clinical pattern is noted in primary pneumococcal peritonitis. The patient appears pale, tired, listless with sunken eyes. Symptoms of upper respiratory infection may precede the abdominal symptoms. Once the abdominal symptoms appear, the clinical picture becomes severe. The abdomen becomes distended, doughy and diffusely tender. Rectal and pelvic examination may show diffuse tenderness.

A pronounced leukocytosis is usually present with counts often greater than 20,000 per cubic millimeter. Blood culture and paracentesis culture may be positive.

The clinical picture is indistinguishable from generalized peritonitis due to ruptured appendix. Similarly, peritonitis, as a complication of genital tract infection should be considered in differential diagnosis. The symptoms of vaginal discharge and diarrhea are occasionally noted in primary pneumococcal peritonitis.[3]

Diagnosis can be established by colpocentesis, paracentesis or surgical exploration. In most of the cases, diagnosis is usually established after surgical exploration.

Abdominal exploration with drainage and antibiotic therapy have been recommended.[1,2] Pneumococcus is an organism sensitive to penicillin and a wide range of other antibiotics.[6] Heavy doses of penicillin are usually recommended.

Summary

A case of primary pneumococcal peritonitis in a

Continued on Page 300

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Gallbladder Malignancy at Stephens Memorial Hospital - 1977

RATNAKER ANDALKAR, M.D., F.A.C.S.

At our hospital of 43 beds serving a population of some 20,000 people, the total number of biliary tree operations were 56. The oldest patient to have a cholecystectomy and choledochoduodenostomy for chronic cholecystitis and choledocholithiasis was 95 years of age. Four other patients, also with obstructive jaundice, proved to have more severe disease. They had malignancy of the gallbladder, Stage IV, and their ages ranged from 78 to 92 years with a mean age of 86 years.

Two of the four patients were admitted with obstructive jaundice and had preoperative diagnoses of gallbladder malignancy made by percutaneous transhepatic cholangiography. This diagnosis was then subsequently confirmed surgically and pathologically. Both had extension of the tumor into the common bile duct and one had involvement of the common hepatic duct as well. In these two cases, bypassing via the common hepatic duct and the jejunum and left hepatic duct and jejunum was carried out. For these two cases, postoperative survival was seven and four months.

A third patient was admitted with upper gastrointestinal bleeding and a barium meal showed a mass in the second portion of the duodenum. Gallbladder malignancy invading the duodenum was the suspected diagnosis and this was confirmed at surgery by surgical biopsy. No definitive procedure could be done because of the extensive nature of the tumor. This patient survived only one and a half months after surgery.

The fourth patient was admitted with a previous history of duodenal ulcer disease. On admission, this patient, too, had obstructive symptoms and a barium meal radiograph showed almost complete obstruction of the duodenum by tumor. An exploratory laparotomy was done and the patient was found to have extensive gallbladder malignancy. The second portion of the duodenum was encircled, causing almost complete obstruction. In this case, a gastrojejunostomy was performed and the patient survived four months after surgery.

In this series of four patients, the mean survival rate was four months after diagnosis. Three of the patients were female and one male; large series of gallbladder malignancy have shown a predelection for women. All four of our patients had adenocarcinoma, three well differentiated and one a mucous secreting anaplastic carcinoma. In a large series from the Mayo Clinic[1], the following cell types were found:

Adenocarcinoma	85%
Adenoacanthoma	12%
Squamous cell carcinoma	3%

Another interesting feature of our four case studies, concern the liver function tests. The two patients with marked obstructive jaundice had elevated SGOT, alkaline phosphatase, gamma GT and bilirubin, but the other two patients who had extensive invasion of liver parenchyma and did have obstructive jaundice, had normal liver function studies. All four patients had had a history of cholelithiasis in the past confirmed in three cases at surgery. In the Mayo Clinic review[1], the ratio of gallbladder malignancy to biliary tract surgery was approximately 1:140. Our experience in the year 1977 was 4:56. At our hospital, gallbladder malignancy ran second among gastrointestinal malignancies, second only to colon cancer cases. The literature reports gallbladder malignancy as ranking fifth or sixth among gastrointestinal malignancies. Among total cancer cases at Stephens Memorial Hospital, gallbladder malignancy ranked as 4%.

Prophylactic cholecystectomy for silent and asymptomatic gallstones was recommended by Glenn and Hays[2] because of their findings that nearly one in five of patients above the age of 65 having had biliary tract surgery have gallbladder malignancy. In our experience, this ratio was 4 and 18. A contradictory view on the basis of autopsy findings was presented by Newman and Northrop that 30% of women over the age of 60 have gallstones at autopsy[3] and that carcinoma of the gallbladder is found in less than 0.5% of all autopsy studies[4]. It is my feeling, however, that malignancy of the gallbladder and its association with gallstones, symptomatic or otherwise, should certainly be a major reason for cholecystectomy. This is supported by a review of Peskin.[5]

In summary, four cases of gallbladder malignancy are presented. They represent an uncommonly high incidence of this gastrointestinal malignancy at our hospital. Despite conflicting views in the literature, it is my feeling that the association of gallbladder malignancy with stones, whether asymptomatic or not, should be a major indication for cholecystectomy.

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17 Winter Street, Norway, Maine 04268

Training for Pediatrics: Practitioners' View

William T. Whitney, Jr., M.D., ★, Linda R. Walters, M.D. ★★ and David G. Watson, M.D.‡

Pediatricians and pediatric educators alike are confused about the future role of the pediatrician. Will he or she practice as a consultant or in primary care or both? Most practitioners believe that they should continue to provide primary care.[1] Recommendations for improved training of pediatricians for primary care have recently become available.[2] They suggest that pediatric residents should have a few patients to care for during training on a continuity basis, be exposed to a model practice setting, and gain experience to preventive care and in managing developmental and emotional problems of children. The incorporation of these changes into existing, hospital-based training programs, however, would involve much expense and possible disruption of well established divisions of responsibility within pediatric departments.

Presently, most of a pediatric resident's time is devoted to tertiary care experience. This training is appropriate for producing pediatric consultants. However, the number of pediatricians has increased rapidly from a ratio of one pediatrician per 5311 children under age 20 in 1964 to one per 3782 in 1972, to a projected one per 1869 in 1985.[3] Numbers then force pediatricians to engage in primary care, despite the unsuitability of their training for this role.

One of the main factors determining the content of residency training is the service need of the medical center hospital. Alternatively, the training experience could depend upon what physicians are going to do after residency. Considerations such as the epidemiology of illness seen in primary care practice, the predictable organizational problems of operating a practice, and the psycho-social determinants of health have been used in developing the curricula of family practice residency programs.[4] As thought is given to improving training in primary care for pediatricians, those involved in setting up training programs might profitably give attention to what the pediatrician does. Also, the practicing pediatrician might have useful suggestions as to the relevancy of training to practive.

As part of a re-evaluation of the pediatric residency of the University of Mississippi Medical Center, we surveyed pediatricians to determine what they did in practice and to elicit their views as to the relevancy of their training to practice. We also hoped that such a survey might provide information about patterns of morbidity and the nature of pediatric practice that are peculiar to the area served by the residency program.

Method

A two-page questionnaire was sent to all practicing pediatricians in Mississippi and to all those who had served as pediatric residents at the University of Mississippi Medical Center. One hundred and forty-two questionnaires were sent out of which 81 were returned. Six were returned but not completed. Nine respondents worked in public health, academic, or specialty settings; because we were studying general pediatric practice, their questionnaires were not analyzed. Of the 66 questionnaires that form the basis for the study, 56 of the pediatricians practiced privately, five in health centers, and five in military pediatrics. Fifty-three pediatricians practiced in Mississippi, and 13 were Mississippi pediatric graduates practicing elsewhere. At the time of the survey, there were 77 practicing general pediatricians in Mississippi.

The questionnaires asked for the respondent's name, age, year of graduation from medical school, type of practice arrangement, number of years of pediatric training and where it was obtained.

To determine the content of practice, we inquired about the amount of time pediatricians devote to certain activities in their daily practice. They were asked to indicate the amount of time given to each activity as one of the following: never, occasional, less than one hour daily, from one to four hours daily, or over four hours daily.

To obtain their views as to the usefulness of their training for practice, the pediatricians were directed to indicate 'the relevance of your training in the area to your pediatric practice'' for each of 26 ''areas of training.'' Relevance was indicated by assigning one of the following descriptions to each of the 26 areas: ''inadequate,'' ''adequate,'' ''excellent,'' or ''excessive.'' We requested that the pediatricians indicate areas of their practice that they particularly enjoyed. Also, general comments were invited.

Results

A. Content of general pediatric practice-

Four of the 66 pediatricians did not complete the section on allocation of time. Several others ommitted a few responses so that the total for each aspect of practice studied fell short of 62 in some instances. The results are summarized in Table 1.

The age of pediatricians did not seem to affect their response as regards allocation of time except that five of the twelve over age 50 spend one to four hours daily as consultants compared to only seven of 47 bet-

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Table 1

	never	occasional	1 hr. daily	1-4 hr. daily	4 hr. daily	total
Newborn care	3	5	20	33	1	62
other hospital care		5	18	36	1	60
behavorial, learning developmental	1	22	22	13		58
chronic illness	2	21	27	8		58
consultant to other physicians	2	13	19	13	2	59
adolescents or adults	5	20	25	10		60
community pediatrics	4	34	12	8		58
well child care		3	7	38	12	60
acute care			2	34	26	62

ween age 30 and 50. Allocation of time did not seem to be related to their ratings of various areas of their training nor to aspects of practice that they enjoy.

B. Relevance of pediatric training to practice-

1. Fifty percent or more pediatricians regard their training in each of the following areas as "adequate:"

chest disease	allergy-immunology
community pediatrics	minor surgery
endocrine-metabolic	multiple handicap
ENT	radiology
gastroenterology	renal-urology
	well child care

2. More than 50% of pediatricians gave "excellent" ratings to three areas of training:

cardiology	36/66
infectious disease	52/66
neonatology	41/66

3. Fifty percent or more of respondents rated their training in the following areas as "inadequate:"

adolescent medicine	36/65
behavioral-emotional	33/66
dermatology	35/66
developmental/learning prob.	41/66
office gynecology	47/64
ophthalmology	33/66
practice management	41/65

4. In six areas, ratings were spread over all four possibilities with none receiving more than 50%:

common ambulatory problems	genetics
hematology-oncology	neurology
orthopedics	

5. Only a few regard areas of training as excessive to their needs in practice:

endocrine-metabolic	4
hematology-oncology	3
infectious disease	2
neonatology	2
gastroenterology and renal	one each

C. Effect of age on ratings by pediatricians of their training-

A correlation was found in the following areas:

		under age 40	over 40
"excellent:"	neonatology	25/31	16/35
	cardiology	20/31	13/35
"inadequate:"	genetics	7/31	21/35

D. Areas of practice regarded as "enjoyable"

We sought to determine if a correlation existed between opinion as to relevance of an area of training and the view of that area as enjoyable in practice.

Table 2

	number of pediatricians who "enjoy"	"excellent in re relevance
infectious disease	37	33/37
neonatology	24	18/24
well child	22	8/22
allergy-immunology	16	8/16
ENT	14	7/14
common ambulatory prob.	11	7/11
neurology	11	8/11
dermatology	11	3/11
hematology-oncology	9	9/9

Discussion

The pediatricians in our study regard themselves as providing care at both the primary level and higher. They spend much time in newborn care, "other hospital care" and as consultants. Of note is that in Mississippi many pediatricians work in secondary level newborn centers. Cardiology, neonatology and infectious disease are viewed as more relevant to practice than other areas of training. It appears in general, therefore, that these pediatricians view their tertiary care training as important to their practice.

Other studies of the content of pediatric practice suggest the opposite. About 40% of pediatricians' time is spent on well child care and more than one-third on minor infectious illness such as bronchitis, otitis, pharyngitis, and gastroenteritis, according to studies of surburban practices.[5,6] In a study of distribution of time in a Kaiser Permanente Group, less than 5% was spent in hospital care of all types. The implication is that pediatricians spend most of their time on trivial illness or well child care. For such a career, training in a medical center hospital might be inappropriate.

Yankauer and others have suggested, however, that rural pediatricians spend more time on complicated illness care than do urban and suburban pediatricians.[7] Fifty-seven percent of the membership of the American Academy of Pediatrics practice in urban areas, 33% in surburban, and only 9% in rural areas.[8] We suggest, therefore, that the training programs whose pedistric graduates are likely to practice

in rural areas preserve some of their tertiary care orientation.

One can also find perhaps a rationale for change from our study. Many areas of training were found to be inadequate for the needs of practice including adolescent care, problems in developmental and behavorial pediatrics, and practice management. Pediatricians in our survey spend considerable time in these areas. Others have likewise reported that pediatricians entering practice were ill-prepared to meet the needs of many of their patients, especially teenagers, those with learning or developmental problems, and those with chronic handicap[9]. Pediatricians have been shown to fail in carrying out recommended procedures that are part of routine health supervision care.[10] Our survey then suggests that the movement to improve the quality of ambulatory pediatric training is amply justified and that pediatricians in practice see the need for improved training in primary care.

The present study can be criticized on the basis of possible inaccuracy of pediatricians' recall of their training. Their views of relevance and quality of training might be biased by their interpersonal relationships with teachers during training and by their being quite interested in certain areas of training and practice that involve actually little of their time in practice. Also, the survey did not yield a clear distinction between the respondents' views of the quality of teaching in an area and its relevance to practice. We might also have compared the attitudes of pediatricians in small towns with those of pediatricians practicing in the larger cities of Mississippi.

Many imperatives need to be considered in planning a pediatric training program including the fact that training is paid for out of income derived from the hospital beds with little left over to pay for training in ambulatory care.[11] Ideally, however, programs which educate pediatricians for a rural area might benefit from study of the special characteristics of the area. These include patterns of morbidity, distance from referral centers, community expectations, and the content of pediatricians' practices. A survey of pediatricians such as the one used in this study is a useful source of data for planning of a training program. Our study suggests that because of the variety of rural practice, pediatricians there could make effective use of experience during training both in tertiary care and in modern ambulatory pediatrics.

Summary

We surveyed practicing pediatricians in Mississippi and graduates of the University of Mississippi pediatric program as to the content of their practice and their views as to the relevance of their training to practice. The results suggest a need (1) for continuance during training of the traditional tertiary care experience, and (2) additional training in ambulatory pediatrics. The training needs for pediatricians in rural areas may be different from the needs of those working in urban or suburban areas.

Continued on Page 302

Tenuate® ℞
(diethylpropion hydrochloride NF)

Tenuate Dospan®
(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION
Brief Summary
INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.
CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).
WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect, rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle, the patient should therefore be cautioned accordingly. *Drug Dependence*: Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression, changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy*: Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children*: Tenuate is not recommended for use in children under 12 years of age.
PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.
ADVERSE REACTIONS: *Cardiovascular*: Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System*: Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache, rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal*: Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic*: Urticaria, rash, ecchymosis, erythema. *Endocrine*: Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System*: Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous*: A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.
DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in midevening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.
OVERDOSAGE: Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976
MERRELL-NATIONAL LABORATORIES Inc.
Cayey, Puerto Rico 00633
Direct Medical Inquiries to
MERRELL-NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215, U.S.A.
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References: 1. Citations available on request — Medical Research Department, MERRELL RESEARCH CENTER, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M.T., O'Dillon, R.H., and Leyland, H.M.: A Comprehensive Review of Diethylpropion Hydrochloride. International Symposium on Central Mechanisms of Anorectic Drugs, Florence, Italy, Jan. 20-21, 1977

Merrell

8-3921 (Y587A)

From the Secretary's Notebook

Summary of 1978 Annual Meeting of the M.M.A. House of Delegates June 10 and 11, 1978 at Rockport, Maine

The 125th annual session of the M.M.A. House of Delegates was held at the Treadway-Samoset Resort in Rockport, Maine with a registered attendance of seventy-four delegates and alternates and thirty-three guests. The first session was convened on Saturday, June 10 at 2:00 P.M., and the second session on Sunday, June 11 at 2:00 P.M. Douglas R. Hill, M.D., President of the M.M.A. called to order the meetings of the House, which were presided over by George W. Bostwick, M.D., Speaker of the House.

Election of Speaker and Vice Speaker of the House of Delegates for 1978-1979 — George W. Bostwick, M.D. was re-elected Speaker, and A. Dewey Richards, M.D. was re-elected Vice Speaker.

Budget for 1979 — As recommended by the Reference Committee, the Budget was *approved* as presented.

Committee on Nominations — A slate was prepared in March at the Interim Meeting of the House of Delegates and presented at this meeting for vote. The following officers were elected:

President-Elect
Brinton T. Darlington, M.D.

Executive Committee
2nd District — William H. Maxwell, M.D.
4th District — O. Thomas Feagin, M.D.
9th District — Harry M. Helfrich, Jr., M.D.

Dr. Gilbert R. Grimes of Lewiston was nominated and elected to complete Dr. Ross Green's term on the Executive Committee for the **7th District.**

The **Standing Committees,** constituted per recommendation of the Committee on Nominations, were *approved*, with the addition of Dr. Peter Leadley to the Peer Review Committee.

Reports (not included in the House of Delegates' folders) —

Assistant Executive Director — Mr. D. Jeffrey Hollingsworth reflected on the past major events and future outlook for the Maine Medical Association, and urged more active participation in Association affairs by every member. His report was *accepted.*

AMA Delegate — Dr. Robert McAfee reported that items expected to be discussed at the upcoming National Convention would include: the National Commission on the Cost of Medical Care, grants for preventive health services, confidentiality of PSRO records, and changes in the AMA Principles of Medical Ethics.

M.M.A. Relationship with Blue Shield — Frederick Holler, M.D., Chairman of a subcommittee of the Committee on Health Care Financing looking into this area, told of concern over changes that have been made in the contract between physicians and Blue Shield. It is his feeling that if physicians were being asked to give up their right of approval power over Blue Shield programs, they should, in return, request that they be released from the obligation of accepting service benefit fee schedules. Dr. Shrier, a member of this subcommittee, reported on sessions held with Blue Shield to discuss their proposal. Mr. Cathcart of BS made a few remarks in response to Dr. Holler's report, pointing out that first, by law, they cannot offer a Blue Shield plan in the State without a third-party contract between the provider and the consumer.

A resolution on this subject appears elsewhere in this summary.

Joint Underwriting Association — Mr. Chester Dosdall, Manager of JUA, reported on their activities in the first 15 months of operation, and responded to several questions from the House.

Building Committee — Dr. John Wickenden, Chairman, reported that the House of Delegates last December instructed his committee to seek land in the Augusta area on which to construct a new building, rather than other alternatives such as renting or purchasing an old building. Several properties were investigated, and the Executive Committee last month unanimously decided to recommend that their first choice be the land available at the Augusta Civic Center complex. Two options were presented to the House of Delegates—the Augusta Civic Center area, and a lot on Capitol Street in Augusta, about ¼ mile from the State House. Cost of this lot, about ⅛ of an acre, is $33,000. This matter was sent to a Reference Committee for discussion and it was their recommen-

dation that the House reaffirm its determination to have its headquarters moved to the Augusta area, which was *approved* unanimously. It was further recommended that the Building Committee of the M.M.A. be authorized by the Executive Committee to purchase a parcel of land in the Augusta Civic Center complex from the Cushnoc Board of Trade, and that the Building Committee, while under the jurisdiction of the Executive Committee, engage a consulting firm and proceed with the formulating of a proposal for the construction of a new headquarters building for the M.M.A.; further, to bring proposed plans back to the Fall Interim Session of the House of Delegates. This was *approved.*

Printed reports not requiring action (resolutions from committees appear elsewhere in this summary) and accepted for information were as follows: Committees — Continuing Education, Health Care Financing, Peer Review, Legislation, Conservation of Vision, Diabetes, AMA-ERF, Maternal and Child Welfare; Reports of Secretary-Treasurer, Executive Committee Chairman and Members, and Delegates to Out-of-State Medical Society Meetings; and School Health Committee report.

Resolutions

Third-party payers — This resolution, submitted by the York County Medical Society and asking that the M.M.A. establish an office to receive, document and arbitrate complaints of physicians regarding their relations with third-party payers, was *defeated.*

Past-Presidents — Presented by the Executive Committee, this resolution was *approved:*

WHEREAS: The 1977 House of Delegates directed that a proposed Constitutional amendment be prepared to enable the Executive Committee to enjoy the counsel of each Past President for an extended period, therefore be it

RESOLVED: That Article VI of the Constitution shall be and is hereby amended to read as follows:

Article VI Executive Committee

The Executive Committee shall consist of the President, President-elect, Executive Director (if a member of the Association), Secretary-Treasurer (if a member of the Association), the delegate(s) and alternate delegate(s) to the American Medical Association, the Speaker of the House, one member from each District, and the immediate Past-President who may, at his/her option, remain a voting member of the Executive Committee in this capacity for a period not to exceed three (3) years. Nine voting members shall constitute a quorum.

L.D. 727 — Presented by the Executive Committee, this resolution was *approved* as amended:

WHEREAS: State law requires that "every state professional society shall establish a professional competence committee of its members pursuant to written bylaws approved by the society's governing board," and

WHEREAS: Such a committee is required to "receive, investigate and determine the accuracy of any report made to the society of any member physician's acts amounting to gross or repeated medical malpractice, habitual drunkenness, addiction to the use of drugs, or professional incompetence," and

WHEREAS: Such assessment of professional competence falls within the purview of the Committee on Ethics and Discipline, now therefore be it

RESOLVED: That subsection B of Section 5 of Chapter VII of the Bylaws shall be and hereby is amended by the insertion, between the current third and fourth paragraphs, a new paragraph to read as follows:

"The Committee on Ethics, Discipline and Professional Competence shall receive, investigate, and determine the accuracy of any report made to the Association of any member physician's acts amounting to gross or repeated medical malpractice, habitual drunkenness, addiction to the use of drugs, or professional incompetence."

Specialty Society Representation in the House of Delegates — Presented by the Executive Committee, this resolution was *approved:*

WHEREAS: It is fitting that deliberations of the House of Delegates should benefit from the counsel of specialty societies, therefore be it

RESOLVED: That Article V of the Constitution shall be and is hereby amended to read as follows:

Article V House of Delegates

The House of Delegates shall be the legislative and policy-making body of this Association and shall consist of 1) Delegates elected by the component societies, 2) the Secretary of each component society (if a member of the Association), 3) the members of the Executive Committee, 4) all past presidents of the Association, and 5) Delegates elected by active medical specialty societies recognized by the Executive Committee of this Association, provided that each member of the House have one (1) vote.

and be it further

RESOLVED: That the present Section 5 of the MEETINGS part of Chapter III of the Bylaws be renumbered Section 6 and that a new Section 5 read as follows:

Section 5. Each medical specialty society which satisfies criteria for eligibility as established by the Executive Committee and as outlined below shall be entitled to one Delegate and one Alternate

Delegate, both of whom shall be members of this Association.

Each such medical specialty society shall

a) have been active for at least one full year and demonstrate, if required by the Executive Committee, that regular meetings to conduct business have been held, and

b) have at least eight (8) active dues-paid members, with a minimum of 75% of all members of record being also members of the Maine Medical Association, and

c) satisfy criteria for activity and recognition of their respective national parent organizations, and

d) satisfy such other criteria as may be from time to time required by the Executive Committee, subject to the approval of this House of Delegates.

The secretary of each such specialty society shall notify the Secretary of this Association by 31 January of each year, in writing, of the names of the elected Delegate and Alternate Delegate for that calendar year.

and be it further

RESOLVED: That Section 1 of the DUTIES part of Chapter III of the Bylaws shall be and hereby is redesignated Section 7, and that the subsequent Sections of Chapter III be renumbered consecutively.

Chairman of Committee on Health Care Financing — This resolution, submitted by the Piscataquis County Medical Society, was *approved:*

WHEREAS: The Committee on Health Care Financing is the only standing committee of this organization to have both geographical and categorical specialty representation, and

WHEREAS: Negotiations with third-party payors have become of major importance to the conduct of business of this Association, and

WHEREAS: The business of this committee frequently requires immediate attention by the Executive Committee, now therefore be it

RESOLVED: That Article VI of the Constitution, entitled "Executive Committee," shall be and hereby is amended by the addition, at the end, of the following sentence:

"The Chairman of the Committee on Health Care Financing shall *ex officio* be a non-voting member of the Executive Committee."

Advisory Members of Committee on Health Care Financing — Presented by the Piscataquis County Medical Society, this resolution was *approved* as amended:

WHEREAS: Both geographically elected members and specialty society Advisory members of the Committee on Health Care Financing participate actively in deliberations of that Committee, and

WHEREAS: It has become custom in this Committee to vote as a body, therefore be it

RESOLVED: That Subsection A of Section 3 of Chapter VII of the Bylaws shall be and is hereby amended by the addition on the last line of the last paragraph the following:

"Each member of the Advisory Committee who is a member of the Maine Medical Association shall be entitled to one vote in the deliberations of the Committee on Health Care Financing and shall be subject to the same rights and duties as the members representing the component county societies."

To Eliminate the Committee on Care of the Disadvantaged — This resolution, submitted by the Committee, was *defeated.* The Reference Committee recommendation that the President and the Executive Committee reorganize and redirect this Committee to make it more responsive to the problems of access to medical care for the disadvantaged, was *approved.* It was further recommended and *approved* that the President appoint an Ad Hoc Committee on Rural Health and to form an eventual standing committee.

Insurance Company — Presented by the Executive Committee, this resolution was *approved* as amended:

WHEREAS: The membership of the Maine Medical Association has indicated that it desires to seek a solution to the malpractice insurance crisis which will assure the continuing availability of such insurance to the membership and to the physicians of Maine, and

WHEREAS: It has been determined that such insurance is not currently available except through a temporary "Joint Underwriters' Association" which expires by law in 1979.

RESOLVED: That the Maine Medical Association endorses the Medical Mutual Insurance Co. of Maine which has been organized for the purpose of providing medical liability insurance to the physicians of the State of Maine.

M.M.A. Lobbyist — A resolution from the Androscoggin County Medical Society, asking that the M.M.A. require that its lobbyists have no commitment to any other group...which could have a conflict of interest, was *defeated.* The following substitute resolution presented by the Reference Committee, was *approved:*

RESOLVED: That the Executive Committee and the Executive Staff of the Maine Medical Association monitor closely the activities of our lobbyist, and if at any time they feel that the interests of the Association are jeopardized, they would have the authority to change the lobbyist.

Third-party payers — Presented by the Cumberland County Medical Society, this resolution was *approved:*

WHEREAS: Most third-party payments occur to physicians from either Blue Shield, State

Department of Health & Welfare or Medicare, and

WHEREAS: The award of Medicare Administration in Maine has recently been awarded to a new agency, Massachusetts Blue Cross and Blue Shield, and

WHEREAS: The cost in physician's offices has escalated remarkably due to administrative attempts to comply with third-party requests.

BE IT RESOLVED: That the Maine Medical Association exert all possible influence with the third-party payers to establish a single unified code systems for identification of physician services and payment of such.

Home Health Care — This resolution, submitted by the Somerset County Medical Society and asking that the M.M.A. regard the physician as the primary appropriate evaluator of a patient's home health care needs, was *defeated* unanimously.

Physicians Negotiating Agency — Presented by the Executive Committee, this resolution was *approved:*

WHEREAS: the State of Maine has continuously underfunded the Medicaid program, resulting in delayed and inadequate payment for all providers; and

WHEREAS: the quality and availability of services to Medicaid patients is compromised by the recent 10 percent fee cut for physicians and the inequities of the new physician fee schedule; and

WHEREAS: the Attorney General of the State of Maine has issued an opinion stating that any cooperation between the Maine Medical Association and the Department of Human Services regarding the establishment of an equitable fee schedule for physicians would be in violation of the Sherman Act; and

WHEREAS: a union is exempt from the provisions of the Sherman Act;

BE IT THEREFORE RESOLVED: That the House of Delegates of the Maine Medical Association constitute and fund the activities of the committee to be appointed by the President charged with gathering information about a physicians' negotiating agency and with evaluating the necessity and desirability of this form of organization to represent physicians in negotiation with the Department of Human Services and other third-party payors.

Mass Screening — Presented by the School Health Committee, this resolution was *approved* as amended:

WHEREAS: It is a goal of both the public and the M.M.A. that each individual within the State should have a personal physician who is the focus of coordinating all medical and medically related services for that individual, and

WHEREAS: In many areas of the State where there are adequate numbers of primary physicians, State agencies are pursuing a multitude of disjointed organ related screening programs, and

WHEREAS: Such programs are a major cause of the fragmentation of individual medical care, therefore be it

RESOLVED: That mass screening of individuals particularly in fragmented organ system screening programs, should be undertaken only with the participation of the Maine Medical Association; and be it further

RESOLVED: That the M.M.A. and local societies develop with the State agencies methods of referral so that each individual will have necessary periodic evaluation as a whole, rather than have the individual's care involved in fragmented disjointed programs. And be it further

RESOLVED: That a copy of this resolution be sent to the Department of Education and Cultural Services, Department of Human Services and each County Medical Society.

Blue Shield — Introduced by the Reference Committee, this resolution was *approved:*

WHEREAS: There exists a deep conflict between the physicians of the Maine Medical Association and Blue Shield, and

WHEREAS: If at all possible, members of the M.M.A. would like to continue discussions with Blue Shield, providing some of the reasons for the conflicting resolves, and

WHEREAS: In the past few days, progress in the discussion with Blue Shield has been made,

BE IT RESOLVED: That further discussions with Blue Shield be held with the Committee on Health Care Financing regarding the Physicians' Blue Shield contract. Further, the House of Delegates shall, at the December 1978 meeting, determine the nature of any future relationship with Blue Shield.

Reports of Reference Committees — Recommendations (not listed elsewhere in this summary) are as follows:

Committee on Allied Health Professions — Report *accepted.*

Burn Advisory Committee — Recommendation that Committee be abolished was *approved* as was the recommendation that physicians representation among the Trustees of the Pine Tree Foundation for Burn Treatment be designated by the Maine Medical Association.

A.H. Robins Community Service Award — The award for 1978 was presented to Dr. Paul Marston of Kezar Falls.

Maine Blue Cross and Blue Shield Award of Appreciation — This year's award was presented to Dr. Johan Brouwer of Rockland.

Out-of-State Delegates — The following delegates spoke briefly of the major problems in

Continued on Page 300

. . . in functional G.I. disorders*

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10 mg./5 ml. syrup, 10 mg./ml. injection

helps control abnormal motor activity
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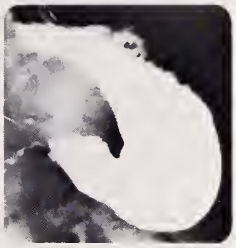
Demonstrated smooth muscle relaxant activity.

In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.

Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

"The correlation of spasm relief and drug given was excellent."

*This drug has been classified "probably" effective in treating certain functional G.I. disorders.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:
King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

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Brief Summary
INDICATIDNS
For use as adjunctive therapy in the treatment of peptic ulcer.
IT SHDULD BE NDTED AT THIS PDINT IN TIME THAT THERE IS A LACK DF CDNCURRENCE AS TD THE VALUE DF ANTICHDLINERGICS/ANTISPASMDDICS IN THE TREATMENT DF GASTRIC ULCER. IT HAS NDT BEEN SHDWN CDNCLUSIVELY WHETHER ANTICHDLINERGIC/ANTISPASMDDIC DRUGS AID IN THE HEALING DF A PEPTIC ULCER, DECREASE THE RATE DF RECURRENCES, DR PREVENT CDMPLICATIDN.

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the following indications as "probably" effective.
May also be useful in the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis, acute enterocolitis, and functional gastrointestinal disorders); and in neurogenic bowel disturbances (including the splenic flexure syndrome and neurogenic colon).
THESE FUNCTIDNAL DISDRDERS ARE DFTEN RELIEVED BY VARYING CDMBINATIDNS DF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIDRATIDN DF ENVIRDNMENTAL FACTDRS.
For use in the treatment of infant colic (syrup).
Final classification of the less-than-effective indications requires further investigation.

CDNTRAINDICATIDNS: Dbstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient; unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis. WARNINGS: In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. PRECAUTIDNS: Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with: autonomic neuropathy; hepatic or renal disease, ulcerative colitis—Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon; hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension; hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.
It should be noted that the use of anticholinergic/antispasmodic drugs in the treatment of gastric ulcer may produce a delay in gastric emptying time and may complicate such therapy (antral stasis). Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur. ADVERSE REACTIDNS: Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia; urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia, increased ocular tension; loss of taste, headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting, impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. DDSAGE AND ADMINISTRATIDN: Dosage must be adjusted to individual patient's needs.
Usual Dosage: Bentyl 1D mg. capsule and syrup: *Adults*: 1 or 2 capsules or teaspoonfuls syrup three or four times daily. *Children*: 1 capsule or teaspoonful syrup three or four times daily. *Infants*: ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 2D mg.: *Adults*: 1 tablet three or four times daily. Bentyl Injection: *Adults*: 2 ml. (2D mg.) every four to six hours intramuscularly only. NDT FDR INTRAVENDUS USE. MANAGEMENT DF DVERDDSE: The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine® (bethanecol chloride USP) should be used.
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their respective states and extended greetings on behalf of their associations: Dr. W. Raymond James, Connecticut; Dr. Frank E. Bixby, Massachusetts; and Dr. Russell Hager, Rhode Island.

Special Guests — The following guests were introduced and spoke briefly: Dr. Robert Hunter, Chairman of the Board of Trustees of the American Medical Association, and Mr. George McLean, new President of Maine Blue Cross and Blue Shield.

Special Memberships — The recommendations by the county societies for special memberships were *approved.*

Stenographic Record — A summary of the proceedings of the House of Delegates is to be sent to county presidents and to the members of the House of Delegates. The complete transcript is on file at the Association's office in Brunswick, where it is available for examination by any member of the Association.

The meeting was recessed at 4:35 P.M. on Saturday, June 10, and was adjourned at 5:05 P.M. on Sunday, June 11.

PATRICIA A. BERGERON
Secretary-Treasurer, M.M.A.

PRIMARY PNEUMOCOCCAL PERITONITIS IN AN ADULT — *Continued from Page 290*

young adult female is present with a review of clinical findings in this condition.

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Annual Meeting Dates For Your 1978 Calendar...

Maine Medical Association
June 10-13
Samoset Resorts, Rockport, Maine

American Medical Association
June 17-22
St. Louis

AMA Delegates Take Significant Step By Cutting Dues For New Practitioners

In voting a 50-percent, one-year cut in AMA membership dues for physicians first entering practice, the Association's House of Delegates did a good turn for all physicians.

The reduction will manifestly bring in more new practitioners, thus giving the AMA a broader base of support and making it more truly representative of the medical profession.

Consequently, the AMA will be even more effective as an organization that sets and protects medical standards, strives for more and better public health, and represents doctors in coping with government, insurers, hospitals, and the media.

The dues cut—adopted at the Association's annual convention in June—means physicians during their often hard-pressed first year of practice will be paying $125 as contrasted with the $250 regular dues and the $35 paid by housestaff.

The membership gain resulting from the dues cut is expected to reach almost 5,000 in five years.

Increased enrollment by physicians of all ages, and in all branches of medicine, is needed if our federation—numerically and financially—is to sustain its strength in the face of constant challenges.

A survey cited in a Board of Trustees report to the House showed that the $250 dues—rather than any lack of awareness of AMA activities—have been a major obstacle to new-practitioner membership.

The report said:

"Ninety-three percent of non-member students, 85 percent of non-member residents, and 88 percent of non-member practicing physicians have specific perceptions of what the AMA does as an organization. For the most part, these perceptions center around lobbying, representing doctors, and medical-education activities."

On the other hand, only 31 percent of the residents surveyed (members and non-members) said they would sign up at the $250 rate, as compared with 42 percent at the $125 rate.

So in numerous instances, the $125 rate will stimulate retention of housestaff and students who have increasingly poured into the AMA since its doors opened to them in 1972 and 1973 respectively. Their combined dues-paying membership jumped from 3,000 in 1973 to 28,094 last year.

They've had the opportunity to see how effective the federation is, and to be influential in that effectiveness. In government and elsewhere, the AMA is respected or attacked chiefly because it is medicine's only general spokesman and doer. And the younger physician's contribution to our impact dates back to our Association's very beginning.

It goes back most notably to Dr. Nathan Smith Davis, who was only 29 when he spun the organizational wheels that made him "the Father of the American Medical Association."

All of us should endeavor to bring more young physicians into the AMA and our state and county medical societies—to help ensure the future vitality and stamina of organized medicine.

Letters to the Editor

To the Editor:

RE: "Asymptomatic Pulmonary Nodule"
by Fennell P. Turner, M.D.,
Volume 69, No. 7, Pages 186-190, 1978

I would like to take issue with two points in the above named article. The first is that the six malignant lesions which were omitted from the series when they were found to be nonresectable at time of surgery should be included with the results. To remove these patients because it was found at surgery that they were not resectable makes little sense. As far as could be told pre-operatively, the patients were resectable and were surgical candidates.

The second point is the advisability of chest radiographs yearly and possibly every 4-6 months. We all agree that patients who will do best with lung cancer are those with asymptomatic pulmonary nodules picked up on routine screening who subsequently prove to have T1NOMO lesions. Unfortunately, the chest radiograph is thus far not proving to be the modality which will result in these lesions being picked up in a significant number. Chest radiographs every 4-6 months have been attempted elsewhere and likewise have not proven beneficial. "Pap smears" may accomplish this but it appears that bronchial washings every 4-6 months are needed; and at this time, this is not practical.

I do not wish to suggest that we stop performing yearly chest radiographs, particularly on those who are at high risk, but I caution against routinely obtaining chest radiographs every 4-6 months until it has been shown that this will be more beneficial.

Jon P. Pitman, M.D.
Radiology and Radiation Therapy
St. Mary's General Hospital
45 Golder St.
Lewiston, Maine 04240

Reply:

I believe I could answer Dr. Pitman's comments in the following manner:

During the preparation of my paper on "Asymptomatic Pulmonary Nodules," I considered the two questions submitted by Dr. Pitman. It was finally decided to limit the study only to Resected Asymptomatic Nodules (See Table 1 of the paper) as I wished to be consistent and use the same 80 patients in each of the following statistical studies: (1) Distribution as to histological diagnosis; (2) Distribution by size; (3) Age; (4) Type of operative procedure; (5) Operative complications and (6) Long term survival. In regards to Dr. Pitman's comments about periodic Chest Radiographs, I would like to point out that I did not recommend that all people have periodic x-ray studies. I had in mind only the advice that one might wish to give the person who smokes. In such

a case, I would recommend firstly "don't smoke." "However, if you insist on smoking at least try to protect yourself by getting an occasional Chest Radiograph" and finally, "If you insist on being a heavy smoker over the age of 50, the best we can do for you is to suggest x-ray studies every 4-6 months because the tumor "doubling time" in the greatest number of cases is from 61-180 days and such rapid growth would best be discovered in an early stage by periodic Chest Radiographs."

FENNELL P. TURNER, M.D.
Chief, Surgical Service
Veterans Administration Center
Togus, Maine 04330

To the Editor:

The Western Electric Company, Inc., has over 180,000 active and retired employees and their dependents who are covered under a Surgical-Medical Expense Plan which is being administered by The Travelers Insurance Company. Prior to 1978, this plan was administered by Blue Shield.

The Travelers is extremely anxious to provide the most efficient claim service possible, in order to best serve the balanced interests of both the claimant and the physician. To meet this objective, we have established a single nationwide claims center, dedicated solely to the Western Electric employee account, in Greensboro, North Carolina. This center is designed to give providers and patients efficient claim processing service and uniform application of the Surgical-Medical Plan benefits as well as Western Electric's Major Medical and Medicare Supplement Plans.

The employee or dependent submits claims directly to this office and is furnished claim forms for that purpose. It is not necessary that the Physician Report that is supplied to Western Electric be used, but any form giving us full information: patient name, diagnosis, charges, and dates of service, will be sufficient for our records.

Any assistance that you can provide in communicating this information to your membership will be greatly appreciated. If we can answer any questions for you, or help in any way, please call us toll free at 1-800-334-2400.

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Manager, Group Claim Dept.
The Travelers Insurance Companies
2120 Pinecroft Rd.
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Greensboro, NC 27407

TRAINING FOR PEDIATRICS: PRACTITIONERS' VIEW — *Continued from Page 294*

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Warnings: Warn patients that mental and/or physical abilities required for tasks such as driving or operating machinery may be impaired, as may be mental alertness in children, and that concomitant use with alcohol or CNS depressants may have an additive effect. Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Usual Daily Dosage: Individualize for maximum beneficial effects. *Oral–Adults:* Mild and moderate anxiety and tension, 5 or 10 mg *t.i.d.* or *q.i.d.*; severe states, 20 or 25 mg *t.i.d.* or *q.i.d.* *Geriatric patients:* 5 mg *b.i.d.* to *q.i.d.* (See Precautions.)

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Necrologies

Charles G. Burr, M.D.
1904-1977

Dr. Charles G. Burr, 73, of Houlton, Maine, died on November 14, 1977 in a local hospital following a long illness.

He was born in Herkimer, New York on October 14, 1904, the son of Charles H. and M. Helena Burr.

Dr. Burr was graduated from Regal-Nausium of Munich, Germany and the University of Maine, and received his medical degree from Tufts University School of Medicine in 1934. Following his internship at the Memorial Hospital in Pawtucket, Rhode Island and the Rhode Island Hospital in Providence, he located in Houlton and practiced there from 1936 until his retirement in 1972.

A senior member of the Aroostook County Medical Society and the Maine Medical Association, he was also a former medical examiner for Aroostook County.

Surviving are his widow, Marion L. Burr of Houlton; one son, Charles M. Burr of Houlton; two daughters, Mrs. Rosamond MacIntosh of Enfield, Connecticut and Mrs. Jane Workie of Philadelphia, Pennsylvania; one brother, Robert of Jacksonville, Florida; three sisters, Mrs. Rosamond Lyons, Miss Aileen Burr and Miss Marguerite Burr, all of East Millinocket; and four grandchildren.

Soleiman Koopal, M.D.
1934-1978

Dr. Soleiman Koopal, 43, of Skowhegan, Maine, died in a Waterville hospital on March 8.

Born in Basra, Iraq on December 10, 1934, he was the son of Hasan and Tooran Koopal.

A graduate of Teheran College, he received his medical degree from Teheran Medical School in 1961, interned at the Mercy Hospital in Pittsburg, Pennsylvania and served a residency in obstetrics and gynecology at the Good Samaritan Hospital in Cincinnati, Ohio. He took a postgraduate course at the Rock Reproductive Clinic in Brookline, Massachusetts.

Dr. Koopal served as a 1st Lieutenant in the Iranian Health Corps from 1966 to 1968 and practiced in Iran until 1971, when he located in Skowhegan.

He was a member of the Somerset County Medical Society and the Maine Medical Association. Dr. Koopal was affiliated with the Redington-Fairview General Hospital in Skowhegan and was a board certified member of the College of Obstetrics and Gynecology.

Surviving are his widow, the former Priscilla Shields of Skowhegan; his mother of Teheran; two daughters, Yazameen and Poohnay of Skowhegan and one sister, Foroogh of Teheran.

Philip H. McCrum, M.D.
1899-1978

Dr. Philip H. McCrum, 78, of South Portland, Maine, died in a local nursing home following a long illness on May 23.

He was born in Portland, Maine on August 27, 1899, the son of Samuel and Clara W. McCrum.

A graduate of Bowdoin College, he received his medical degree from Harvard Medical School in 1925. Following his internship at Boston City Hospital, Dr. McCrum located in Portland in 1928 and practiced there until 1974, retiring because of ill health.

He served in the U.S. Army Medical Corps during World War II, retiring with the rank of Colonel.

An honorary member of the Cumberland County Medical Society and the Maine Medical Association, he received a 50-year pin in 1975. He was also a member of the American Medical Association, the Maine and New England Obstetrical and Gynecological Societies and the Maine Medical Center staff where

Continued on Page 325

The Journal
of the
Maine Medical Association

Volume Sixty-nine | Brunswick, Maine, November 1978 | Number 11

Dedication to Dr. Morrison

Dr. Robert M. Morrison was a member of the Maine Medical Center and Mercy Hospital Departments of Obstetrics and Gynecology from 1962 until 1976. To those of us who knew him he will be remembered as a friend, a teacher, and as a physician who cared deeply for his patients. His ever present kindness and his high moral and ethical standards continue to serve as a model for us all.

We who were his friends wish to dedicate this issue of *The Journal of the Maine Medical Association* to his spirit and memory.

DMcC
JZ

Changing Patterns in an Obstetrical Population: Ten Years' Experience

David C. Ernst, M.D.*, Niki Saltzer, RN, BSN, EdM**
and John Zerner, M.D., FACOG, FACS†

Introduction

Over the past decade there have been changes in certain characteristics of obstetrical patients in their labors and deliveries. These changes reflect a variety of trends in obstetrical care and in population trends in general, including more sophisticated technology and knowledge of maternal-fetal medicine, emphasis on population control, higher divorce rates, and increased patient demands for improved obstetrical care and outcome. Some of the changes—total number of deliveries, gravity and pariety of obstetrical patients, and type of delivery and anesthesia—were reviewed at the Maine Medical Center for two separate years, ten years apart.

Materials and Methods

Information listed in the delivery book kept by the obstetrical nurses on all labors and deliveries occurring at Maine Medical Center were reviewed for two separate one-year periods: October 1, 1964 through September 30, 1965, compared with October 1, 1974 through September 30, 1975. Statistics are kept on a yearly basis from October 1 to September 30 of the following year. Data on the following were collected for the two respective years: total number of deliveries at Maine Medical Center, gravity and pariety of patients, marital status, private versus service or clinic status, type of delivery including Cesarean section, and type of anesthesia used for delivery. These data are summarized in Tables 1-4.

Table 1

Parity, Marital Status, and Private Versus Clinic Status of Patients

		1964-65 No.	1964-65 Percent	1974-75 No.	1974-75 Percent
Total Number of Deliveries		1570		1577	
Parity:	Para I	488	31.1	737	46.7
	Para II	370	23.6	502	31.8
	Para III	275	17.5	212	13.4
	Para IV	195	12.4	86	5.5
	Para V or greater	242	15.4	40	2.5
Marital Status:	Married	1461	93.1	1457	92.5
	Single	109	6.9	83	5.3
	Separated	0		10	0.6
	Divorced	0		26	1.6
	Widowed	0		1	
Patient Status:	Private	1223	77.9	1168	74.1
	Clinic	316	20.1	395	25.0
	No Prenatal Care	31	2.0	14	0.9

Table 2

Type of Delivery

	1964-65 No.	1964-65 Percent	1974-75 No.	1974-75 Percent
Spontaneous Vaginal	786	50.1	763	48.4
Low Forceps	635	40.4	509	32.3
Mid-Forceps	9	0.6	39	2.5
Cesarean Section (Total)	140	8.9	266	16.9
Cesarean Section (Primary)	79	5.0	171	10.8

Results

A. Number of Deliveries

In the year 1964-65, there were a total of 1570 deliveries, compared to 1577 in 1974-75 (Table 1). This represents a fairly steady number, with a low of 1417 in 1966-67 and a high of 1807 in 1970-71, and a yearly average of 1582 over the last eleven years. Incidentally, during the latter four years, 1972-76, the total number of deliveries has increased yearly to 1710 in 1975-76.

B. Parity

It seems that an increasing percentage of those delivering are having their first child. To determine if this is true, the parity of delivering mothers was compared for the two years in question. Parity is defined as the number of pregnancies carried to the stage of viability and delivered, regardless of the number of fetuses or stillborns.[1] The data in Table 1 show that in 1964-65, 488 or 31.1% of deliveries occurred in primiparous patients, in contrast to 737 or 46.7% ten years later. Secundiparas accounted for 23.6% and 31.8% of the parturients for the two respective years. Parity of five or greater occurred in 15.4% of deliveries in 1964-65, and only 2.5% ten years later.

C. Marital Status

Another interesting feature of parturients is their marital status. In 1964-65 there were 109 single patients; the 1461 remainder were married and there were no recorded deliveries in separated, divorced or widowed women. In 1974-75, only 83 of 1577 patients were single but there were an additional 10 who were separated, 26 divorced and 1 widowed.

D. Private versus Clinic Status

The patients were also divided into private versus

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TABLE 3

TYPE OF ANESTHESIA FOR VAGINAL DELIVERY

	1964-65		1974-75	
	No.	Percent	No.	Percent
General	1137	80.0	16	1.2
Spinal	184	12.9	1002	76.4
Pudendal	12	0.8	23	1.8
Local to Perineum	36	2.5	186	14.2
None	61	4.3	84	6.4

TABLE 4

TYPE OF ANESTHESIA FOR C-SECTION

	1964-65		1974-75	
	No.	Percent	No.	Percent
General	11	7.9	45	16.9
Spinal	114	81.4	209	78.5
Failed Spinal Attempts	15	10.7	12	4.5

clinic or service, with results listed in Table 1. Clinic patients have comprised a small but steady number of total patients delivering, with 20.1% having that status in 1964-65, and 25.0% ten years later. Interestingly, 2.0% of patients had no prenatal care in 1964-65 and only 0.9% in 1974-75.

E. Type of Delivery

Numbers and percentages of the different types of deliveries are listed in Table 2. Four types of deliveries were recorded: spontaneous vaginal, low forceps, midforceps, and Cesarean sections (broken down into total and primary Cesarean sections). Approximately half of the deliveries for both years were spontaneous vaginal ones (50.1 and 48.4%, respectively). The low forceps rate declined from 40.4% in 1964-65 to 32.3% ten years later, despite the large increase in the use of spinal anesthesia for vaginal deliveries (see below). The midforceps rate actually increased from 0.6% to 2.5% of the vaginal deliveries, or nine midforcep deliveries in 1964-65 and 39 recorded in 1974-75. The reasons for this are unclear.

The Cesarean section rate reflects the nationwide increases over the past few years. There were 140 Cesarean sections in 1964-65 for an overall rate of 8.9%, with a primary rate of 5.0%. This had doubled ten years later, the rates being 16.9% and 10.8% for overall and primary rates, respectively. This compares with the Cesarean section rate today in large university centers, where up to 20% of deliveries are by Cesarean sections.

F. Type of Anesthesia

The last characteristic of labor and deliveries compared for the two respective years was the type of anesthesia used for delivery. Spinal anesthesia has been available at Maine Medical Center for many years and has been traditionally given by the Anesthesiology Department. Epidural and caudal anesthesia have not been readily available and hence the various types of anesthesia recorded include general, spinal or saddleblock, pudendal block, local infiltration to the perineum, and no anesthesia at all. Table 3 lists the different types and percentages used for vaginal deliveries, with some very interesting changes. Of the 1430 vaginal deliveries in 1965-66, general anesthesia was used in 80.0%. Virtually all of the general anesthesia for deliveries was administered by mask and without endotracheal intubation. Most cases were some combination of nitrous oxide, cyclopropane, and oxygen, with the majority being a mixture of cyclopropane and oxygen. The next most popular anesthesia was spinal or saddleblock, used in only 12.9%. These are true spinals in that the anesthetic is given with the patient in the lateral position and total motor and sensory block from the umbilical level downwards is produced. No anesthesia was used in 4.3%, local in 2.5%, and pudendals only 0.8%. Ten years later the situation had remarkably changed in that only 16 of the 1311 patients delivering vaginally had general anesthesia for a rate of 1.2%. In contrast, spinals were used in 76.4% or over three-fourths of all vaginal deliveries with locals accounting for an increased 14.2% and the no anesthesia and pudendal rate about the same. Many factors have accounted for these changes and will be speculated upon later.

Anesthesia for Cesarean sections has not changed significantly at Maine Medical Center over the ten year period in study. Spinals have been the predominant method, accounting for a significant 81.4% in 1964-65 and 78.5% in 1974-75. General anesthesia was used in the remainder including the 10.7 and 4.5% of the totals for the two years respectively in which spinal anesthesia was first attempted but failed.

DISCUSSION

The total number of deliveries per year at Maine Medical Center during the years 1964 through 1976 has not reflected the nationwide trend of decreasing numbers, and in fact the trend has been just the opposite the last four years. After a peak of 1807 deliveries in 1970-71, there was a drop two years in a row to 1462 in 1972-73. However, this has increased each year since, with 1500 deliveries in 1973-74, 1577 in 1974-75, 1710 in 1975-76, and 1800 in 1976-77. A full explanation of this is unclear but in part may be related to three factors. The nationwide decline in the birth rate has necessitated closure of some smaller obstetrical units, and patients normally delivering in such places must travel farther to regionalized centers such as Maine Medical Center. The latter may not be a significant factor in the increased number of deliveries at Maine Medical Center because there have been very few, if in fact any, closures of obstetrical units in the greater Portland area or surrounding towns. Secondly, and most importantly,

there has been an increased number of statewide referrals of high-risk obstetrical patients to Maine Medical Center because of its neonatal intensive care center, which officially opened in 1973. Lastly, although women are having fewer babies per person, there are simply more women having babies.

Just under one-third (31.1%) of women delivering in 1964-65 at the Maine Medical Center were having their first baby. In 1974-75 this had increased to nearly one-half or 46.7%. This compares interestingly to a large center such as Park Memorial Hospital in Dallas, Texas, where only one-fourth of the 7,000 women delivering there in 1964 were primiparas, and this likewise increased to one-half in 1974.[2] Since a given woman has fewer children today than her counterpart ten or more years ago, it stands to reason that a higher percent of parturients today will be primiparous women.

The slight decrease of patients who were never married from 109 in 1964-65 to 83 in 1974-75 is difficult to explain, but perhaps reflects a balance between several separate factors. The first of these is the increased availability of elective abortions in recent years, which would tend to decrease the number of never married patients having babies. On the other hand, recent studies have shown an increasing number of teenagers having babies and fewer of these females are marrying to resolve the problems of ilicit pregnancy.[3] The stigma of being single and giving birth is not nearly so great as it was a decade ago. Also the increased incidence of divorced and separated women easily accounts for the appearance of this group of women having babies, as compared to its rarity in 1964-65.

Statistics on the types of vaginal deliveries reflect some interesting and paradoxical changes. The spontaneous delivery rate for the two periods is nearly identical (50.1 and 48.4%, respectively) despite a dramatic change from general to spinal anesthesia used for delivery. This is not so surprising as is the actual decreased low forceps delivery rate from 40.4 to 32.3%, since it is well established that the use of regional anesthesia increases the incidence of forceps delivery.[4] The efficacy of pushing and expelling the baby's head is markedly reduced with spinals because of the mother's lack of sensation and hence inability to coordinate the bearing down effort, so the application of forceps could be necessary more often. However, this would also apply if the mother were asleep, so spinals should only increase the forceps rate when compared to local anesthesia and not compared to general anesthesia. Since 92.9% of deliveries were either by general or spinal anesthesia in 1964-65, local in only 3.5% and spinal or general accounted for only 77.6% in 1974-75 but local in 16.0%; this could easily account for the actual decline in low forceps delivery rate. The total forceps rate at Maine Medical Center of 34.8% is comparable to the nationwide estimates of from one-fourth to one-third of all deliveries aided by forceps.[5] An interesting

Continued on Page 307

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Brief Summary
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DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg tablet three times daily, one hour before meals, and in midevening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.
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study by Nyirjesy and Pierce in 1964 compared perinatal mortality and maternal morbidity in spontaneous vaginal versus forceps deliveries, and they found no statistically significant differences between the two groups.[6]

The doubling of the Cesarean section rate at Maine Medical Center over ten years from 8.9 to 16.9% reflects a nationwide trend.[5] There has been a slow steady rise over many years, but a much more precipitous rise in the past ten to twelve years. For example, at a New York (lying-in) hospital, the Cesarean section rate in 1932 was 2.5%, in 1963 5.1%, and in 1972, 13.3%. At Johns Hopkins Hospital in 1972-73, the rate was 15.4%. In many referral institutions the rate has risen to nearly 20%. The reasons for the increase are multiple.[7] Better surgical technique and instruments, better antibiotics, and improved anesthesia leading to a decreased maternal morbidity from abdominal operations are only partly responsible. An increasing amount of data showing conclusively that fetal morbidity and mortality is higher with difficult forceps deliveries and vaginal breech deliveries, especially in premature infants, has been the major factor in the increased incidence of Cesarean section. Use of electronic fetal monitoring and recognition of patterns of fetal distress have contributed only slightly to the raised incidence, and this usually only transiently with the introduction of such equipment until familiarity with the significance of various fetal heart rate patterns is achieved. Use of fetal scalp pH has stemmed this initial increase. Improved prenatal nutrition and larger birth weight of infants has undoubtedly increased the occurrence of fetopelvic disproportion. Lastly, the concept of every baby being a "premium baby" because of fewer children per family and hence more reluctance to tolerate any avoidable birth injuries is felt by some to influence the decision toward Cesarean section. At referral centers such as Maine Medical Center, the Cesarean section rate is higher simply because of the increased numbers of referral of high-risk obstetrical problems such as placenta previa, multiple gestation, and premature labor with breech presentation.

The most dramatic change in characteristics of obstetrical patients over the decade 1965 to 1975 has been the type of anesthesia used for vaginal delivery. The marked reduction in the use of general anesthesia at Maine Medical Center again reflects nationwide trends, and the reasons are many. Part of the decline is obviously due to the more recognized maternal morbidity of general anesthesia without intubation in laboring patients, in whom gastric emptying time is extremely delayed and the risks of aspiration extremely high. At the present time, virtually no parturients are put to sleep at Maine Medical Center without endotracheal intubation. Another major reason for the decline in the rise of general anesthesia has been the evolution in less than a generation of an entirely different philosophy towards childbirth. More women want to experience labor and participate in the birth of their child, and hence be awake for the entire process. This not only means less general anesthesia but also less usage of drugs in labor such as scolpolamine and large doses of narcotics. Increase in the usage of local anesthesia reflects an even stronger desire, encouraged by childbirth education classes such as LaMaze, to participate more fully in parturition.

Summary

Certain characteristics of parturients at Maine Medical Center have been compared for two separate years ten years apart, 1964-65 with 1974-75. These included total number of deliveries, gravity and parity, marital status, private versus clinic status, type of delivery, Cesarean section rates, and type of anesthesia for delivery. The most striking differences seen were the increase in Cesarean section rate from 8.9 to 16.9%, the dramatic change in type of anesthesia from 80% general to nearly 80% spinals for vaginal deliveries, and the slight decline in the low forceps delivery rates.

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Changes—Believe Me, I've Seen Some

FRANCES L. ROBINSON, R.N.*

One of Webster's definitions of CHANGE is "to alter or make different." As a member of "The Old Guard", I have seen a tremendous amount of change in obstetrical nursing, during the last twenty years, since entering the ranks, fresh from a three year diploma program.

My first recollection of a labor room, is a large single room with five beds, each with cribsides all around. The labor patient was brought to this room from the Maternity Unit on the fifth floor of the Maine General Hospital. Labor and delivery was on the seventh floor. The patient would not see her husband, or other family members, until after she had delivered. No outsider was permitted to enter these hallowed halls.

As a part of the admission, a rectal exam was performed, usually by a nurse. Once this technique is mastered, it is never forgotten. The first few months of experience helped to develop a very keen sense of observation, as these exams were not too reliable. After a full perineal prep and an S.S. enema, the patient was usually ready for medication. Medication, twenty years ago, usually consisted of Intravenous Barbituates and Intramuscular Scopolamine. Then the patient was transferred, in her bed, to the hallway outside of the delivery room. From here on until delivery, the nursing care essentially was custodial, in that one alertly observed the progress of labor while attempting to keep the patient in bed, and prevent her from hurting herself. The fetal heart tones were checked at half hour intervals with a bell stethescope or "Big Ben", the Leffscope. Who had ever heard of continuous fetal monitoring?

To induce labor, fractional doses of Pitocin® were administered. Dosages were started at ½ minim, to be increased by ½ minim, up to 3-4 minims. These were given by either Subcutaneous or Intramuscular routes. Intravenous Pitocin was rarely ordered.

When delivery was imminent, the physician was notified. The patient's legs were never held together to prevent delivery; therefore, if the attending physician had not arrived when everything was ready, the delivery was performed by a resident physician, or an obstetrical nurse, if the need arose.

As a "well trained" OB nurse, I was able to administer Drop Ether when the need arose. Fortunately, there was a Nurse Anesthetist on call. The anesthetist administered Cyclopropane or Nitrous Oxide and Ether, to make the patient "comfortable." This type of anesthesia was a blessing, as we used Tincture of Zephiran® for the perineal spray. The patient needed to be asleep. Also, at this time very little was done about the conductivity problem and the danger of explosion.

I have all the praise in the world for the Nurse Anesthetists. They could control a patient with the touch of an artist. When relaxation was needed for a Breech, the anesthetist could achieve this very readily.

The delivery room nurse was well acquainted with the Emerson Resuscitator. Many newborns needed resuscitation, to some extent. The baby was placed in an open crib, and, the nurse took over. She placed a metal clamp on the umbilical cord, being careful not to clamp it onto her finger. Then silver nitrate drops were instilled into the baby's eyes, and rinsed out with distilled water. After identification, the baby was whisked down to the nursery on the fifth floor. There the father and grandparents could view the baby, but, only through the window. Mother saw baby several hours later when she awakened.

Then after the delivery room was cleaned, the mother was taken down to her room, and if there were no other patients, we had "routine duties." These consisted of washing, drying, powdering and sterilizing gloves—if they were left in the sterilizer too long, they were a sticky, smelly mess. Overcooked rectal tubes were in the same class. Other duties were folding linen and autoclaving the delivery packs. Needles and syringes were washed and autoclaved also.

One of the "prize" tasks was washing blood clots off the linen. Another was taking the placentas down seven floors and outside to the incinerator. The Porter could not be expected to handle those things, but, nurses could!

When delivery room duties were completed, Peri-Pads had to be wrapped and autoclaved for the Post Partum floor, and then the nursery linen had to be folded.

This went on for several years, until we started to meet the "New Breed" of physicians and became aware of different and better techniques.

The first change that I recall, was a new outlook on medication and anesthesia. This effected the nurses, as we now could converse intelligently with our patients during their labor. As a result of this, we found ourselves in a more supportive role. Patients started having Saddle Block Anesthesia delivery. We now had to share that baby with mother. She was AWAKE!! We also found that the use of the Emerson Resuscitator was decreasing.

The next boon to nurses was the advent of disposables. This includes delivery packs, needles,

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Changing Concepts of Pelvic Inflammatory Disease

David L. B. Eldredge, M.D.* and Harry W. Bennert, M.D.**

In the past, when discussing non-tuberculous salpingitis, authors have concentrated on gonococcal pelvic infections, giving the impression that pelvic inflammatory disease was exclusively a gonococcal infection. Numerous studies in the last ten years employing careful culturing techniques, laparoscopic examination of the pelvis with culture of the fallopian tubes, and culdocentesis for cultures of the peritoneal fluid, however, have revealed the polymicrobial nature of the disease. Long term follow-up of these patients, coupled with laparoscopy and other diagnostic techniques, have also given insights into the long range morbidity of this disease in the antibiotic era.

For the purposes of this review we shall use Hager's definition of pelvic inflammatory disease as "inflammation of the fallopian tubes secondary to ascending bacterial infection unrelated to surgery or childbirth."[8] In most cases, we will be referring to the acute form of endometritis-salpingitis-peritonitis in our discussion.

It is not known how prevalent pelvic inflammatory disease actually is. In recent years, approximately one million cases of gonorrhea have been reported annually in the United States. However, the Center for Disease Control in Atlanta estimates that probably a more realistic figure is two and a half million cases of uncomplicated gonorrhea per year. If one assumes that 10% to 15% of women with gonorrhea develop pelvic inflammatory disease and that gonococcus is present in 40% of the cases of pelvic inflammatory disease, then one could extrapolate that there are around 250,000 cases of pelvic inflammatory disease in this country annually.[8,9,10,24,26] Clearly then, this is a prevalent disease and one that is likely to be seen frequently by the primary care physician as well as the gynecologist. It is therefore important that the bacteriology, pathophysiology and sequelae of the disease be understood by any physician caring for the sexually active female.

The work of Curtis in the 1920's, 1930's and 1940's, which involved culturing of surgically removed fallopian tubes from patients with salpingitis, revealed a high rate of recovery of Neisseria gonorrhoeae.[10,19,24] This led to the concept that practically all cases of salpingitis were caused by gonococcus. In the 1970's, studies by Eschenbach, Monif, Chow, Swenson and others, involving careful bacteriologic examination of the peritoneal fluid in patients with pelvic inflammatory disease, made it clear that most cases of pelvic inflammatory disease were polymicrobial in nature. Eschenbach, et al, in 1975,[4] performed cervical culture and culdocentesis in 204 women with pelvic inflammatory disease and cultured gonococcus in only 91. Of the patients with positive cervical cultures for gonococcus, only 38% had positive cultures for gonococcus in the peritoneal exudate. Moreover, gonococcus was not found in the peritoneal exudates of the patients with negative cervical cultures for gonococcus. The most common bacteria found were Bacteroides fragilis, peptostreptococci and peptococci, and most of the peritoneal exudates were mixed cultures. Chow, et al in a similar study[12] also found a mixed flora in the peritoneal exudates with anaerobes, aerobic streptococci and coliforms predominating. Another significant finding was that the bacteria cultured from the cervix did not correlate well with the bacteria in the peritoneal exudates. In Chow's series of 20 patients, only 13 had gonococcus present in the cervix. Other studies also showed multiple bacteria present in the peritoneal exudates of both gonococcal and non gonococcal pelvic inflammatory disease.[19,26,28]

Data from these more recent studies clearly demonstrate a need to revise our concept of pelvic inflammatory disease. Although Neisseria gonorrhea is probably implicated in about 40%[4,26] of cases, its role in the others is open to question. Other studies have suggested that organisms such as Mycoplasma and Chlamydia may also play a role in initiating pelvic inflammatory disease.

Most investigators agree with the following proposed mechanism for the pathogenesis of gonococcal pelvic inflammatory disease.[6,8,10,24,24,26] The gonococcus is inoculated into the female vagina by an infected male, before and during ejaculation. The gonococcus soon thereafter is found to reside in the endocervix, urethra, periurethral glands, Skene's glands and Bartholin's glands. The fact that gonococcus requires a pH of 7.2 to 7.6, cannot invade stratified squamous tissue well, but readily penetrates columnar or transitional cells is consistent with these findings. The gonococci finding themselves on the vulva or in the vagina probably soon die in a hostile environment. There is also the possibility that some gonococci directly attain access to the fallopian tubes by attaching to the tails of spermatazoa and "hitch hiking" along with the sperm.[24] This mechanism may be involved in women who become symptomatic just

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several days after exposure. However, most gonococci reside in the comfortable environment of the endocervical canal, along with many other potential pathogens, causing at most a cervicitis and cervical discharge until the ecology of the genital tract changes allowing spread to other susceptible areas. For the gonococcus, the most opportune time to spread to the fallopian tubes appears to be menstruation. In fact, up to 75% of the cases of gonococcal pelvic inflammatory disease occur in the perimenstrual period.[26] Some of the proposed mechanisms of spread are that the sloughed endometrium is no longer protective and so the gonococcus is free to spread along the surface of the endometrial cavity to the fallopian tubes. Also, the menstrual blood provides good culture medium and then uterine contractions during menstruation reflux this infected blood into the tubes. Whatever the mode of transport, the gonococcus then achieves contact with the vulnerable mucosa of the tubes and an endosalpingitis begins. Ciliary motility is lost and epithelial cells destroyed resulting in an endosalpingitis with purulent exudate within the tubes. It is presumed that secondary infection then occurs by other organisms from the endocervix or from close lying bowel which is already inflamed by the neighboring salpingitis. Thus, by the time the patient is symptomatic from the peritonitis, a mixed infection is present. After several days, the Neisseria may even be crowded out by these other pathogens and thus be no longer present by the time the patient seeks medical help and is cultured. This concept is supported by the fact that Lip and Bergoyne[26] isolated a greater percentage of gonococcus from peritoneal exudates in women with recent onset of symptoms than from women with symptoms of longer duration. Another hypothesis for the low recovery of gonococcus from the peritoneal exudate may be that Neisseria cause an endosalpingitis preferentially and are less favored on serosal surfaces. Whatever the mechanism, a polymicrobial infection is present and a variety of organisms contribute to tubal damage.

The weight of evidence implicates Neisseria gonorrhoeae as a major initiator of salpingitis.[24] Yet recent studies suggest that other organisms may be involved, either synergistically or alone.[2,4,19,24,26,28] In 1975, several studies showed a high rate of recovery of Chlamydia trachomatis in the endocervix of sexually active women. In 1977, Mardh, et al,[14] in Sweden, demonstrated a high yield of Chlamydia trachomatis from the endocervix and endosalpinx of women with laparoscopically proven salpingitis. (It is of interest that all those with positive tubal cultures had negative cul-de-sac aspirate cultures). Moreover, Eschenbach[4] found a rise in Chlamydia trachomatis antibody titers in 17% of women with gonococcal pelvic inflammatory disease and 20% of women with non-gonococcal pelvic inflammatory disease. That Chlamidya trachomatis is sometimes present in pelvic inflammatory disease is confirmed, but whether it is important in the initiation of upper genital infection still requires further proof.

Mycoplasm hominis has also been found in patients with pelvic inflammatory disease. It has been shown that positive cervical cultures for Mycoplasma are more frequent as the number of sexual partners increases, and that Mycoplasma is often found in males with non-gonococcal urethritis,[4,14,16,21] Moreover, Mardh and Westrom[14] found cervical and fallopian tube cultures positive for Mycoplasma in 8% of patients with salpingitis. All of these patients had non-gonococcal salpingitis. On the other hand, Eschenbach, et al[4] found that rises in antibody titers to Mycoplasma were more common in gonococcal rather than non-gonococcal salpingitis. There have also been a few cases of pelvic inflammatory disease in which fallopian tube cultures and pelvic abscesses have only cultured out Mycoplasma. Furthermore, experiments with cows have shown that salpingo-oophoritis can be caused by Mycoplasma alone.[21] Whether or not Mycoplasma alone causes salpingitis in humans may never be proven, but the weight of current evidence suggests that it can.

Recently, there has been some controversy over the significance of the I.U.D. as a risk factor in salpingitis. The subject is too lengthy to go into detail here, but several studies have shown an approximately five-fold increase in the risk of developing both gonococcal and non-gonococcal salpingitis.[5,7,10,20,25] Those with I.U.D.'s tend to have more serious infections and some I.U.D. wearers have unilateral salpingitis with a tendency to develop unilateral tubo ovarian abscesses. The mechanism for this is not known.

Several follow-up studies on women with prior pelvic inflammatory disease have shown an alarming incidence of infertility and chronic pelvic pain. In one study, Westrom[33] relaparoscoped 415 women with previously laparoscopy proven salpingitis approximately ten years later. Of these, he concluded that 17% were infertile because of tubal occlusion and 18% had chronic pelvic pain attributable to prior salpingitis. By splitting up this group, he also concluded that infertility was more common with those with a history of more than one episode of salpingitis. Those with three or more episodes had a 75% infertility rate. Of those in the whole group who did become pregnant, 4% had ectopic pregnancies. Other authors have agreed with these findings and have suggested that early treatment may improve later fertility.

Clearly there is a need for prompt and adequate treatment. This depends first on accurate diagnosis. At times this can be difficult. The typical findings of fever, lower abdominal pain, vaginal discharge, dysfunctional bleeding, and bilateral adnexal and uterine tenderness on exam does not always indicate pelvic inflammatory disease. Likewise, leukocytosis and elevated sed rate are not always present. However, gastrointestinal symptoms such as vomiting may be present, and hepatic tenderness may be present as in the Curtis-Fitz Hugh Syndrome of gono-

coccal peri-hepatitis. Also adnexal tenderness may be unilateral in pelvic inflammatory disease. There is much overlap of signs and symptoms between salpingitis and other intra-abdominal pathology. Jacobsen, et al[26] found that of women with classical criteria for salpingitis admitted with that diagnosis, only 65% proved to have salpingitis by laparoscopy. Therefore, for definitive diagnosis of pelvic inflammatory disease laparoscopy is needed. In fact, in any patient where the diagnosis of pelvic inflammatory disease is subject to question or in any patient with presumed pelvic inflammatory disease who fails to improve on antibiotics, laparoscopy is indicated.

Recently many investigators have proposed that culdocentesis be performed on all women suspect of having pelvic inflammatory disease.[4,19,26] If no fluid is obtained on aspiration, then lavage is done with saline and then aspirated. The aspirate is then cultured aerobically, anaerobically, and on Thay-Martin Medium. The aspirate is also gram stained and the presence of white cells and bacteria indicates the presence of salpingitis. However, this is not always reliable as the following case demonstrates:

A 26-year-old white female Gravida I, Para I presented with a four hour history of fever, chills, nausea, vomiting and left lower quadrant pain. Her last menstrual period was three weeks previously and was normal. She denied vaginal discharge. On physical exam, she had normal bowel sounds and lower abdominal tenderness. Pelvic exam revealed a clean cervix with I.U.D. in place, a normal sized tender uterus, and bilateral adnexal tenderness without masses. The I.U.D. was removed. Culdocentesis revealed 2cc of cloudy fluid and a gram stain showed gram negative bacilli and neutrophils. The W.B.C. was 15000 and the sed rate 4. Temperature was 37°. She was admitted with the diagnosis of P.I.D. and started on intravenous Ampicillin. The abdominal pain remained unchanged and the patient remained afebrile until 48 hours after admission when she developed sudden onset right lower quadrant pain, chills, and fever to 38.9°. Laparoscopy at this point revealed a normal left fallopian tube, an inflamed right fallopian tube and an inflamed perforated appendix. Appendectomy was performed and the patient recovered uneventfully.

As can be seen, the positive culdocentesis was misleading. This is not to say that culdocentesis is not important. It should be done on almost all patients with suspected pelvic inflammatory disease, especially those with peritoneal signs. But as with any other test, the interpretation of the findings is what counts.

Once the diagnosis of salpingitis is assumed, then prompt antibiotic treatment is indicated. The ideal antibiotic regimen is one which is non toxic, has few side effects, and effectively kills the pathogens involved. Unfortunately, because of the polymicrobial nature of this disease, complete coverage is not possible. The current recommended treatment schedules all assume a gonococcal etiology for pelvic inflammatory disease. As we have seen, this is not always the case. Certainly because almost half of the cases of pelvic inflammatory disease are gonococal, adequate treatment for gonococcus is needed. But broad spectrum coverage is also needed. The high doses of penicillin recommended are fairly broad spectrum. The streptococci, some gram negatives and many anaerobes are susceptible. However, Bacteroides, Chlamydia and Mycoplasma go uncovered. Using Ampicillin or Amoxicillin broadens the gram negative coverage, but still does not eradicate Chlamydia, Mycoplasma, or Bacteroides. Tetracycline is effective against most Chlamydia and Mycoplasma and has good gram negative coverage. However, it is not as effective as the penicillins against the streptococci and does not get Bacteroides. Also, it is contra-indicated in the pregnant patient. Erythromycin is broad spectrum but lacks efficacy against the gonococcus[31,32] and Bacteroides and is poorly tolerated. The cephalosporins are broad spectrum antibiotics but show no advantage over the penicillins in clinical studies and again do not cover Bacteroides.[35] Also, there is a 15% chance of allergic reaction in the patient who is allergic to the penicillins. Clindamycin, chloramphenicol, and Carbenicillin are effective against Bacteroides, but their toxicity make them second line drug choices.[29]

Clearly there is no one ideal antibiotic. Fortunately, eradicating most of the bacteria involved usually affords a clinical cure.[3,10] Also, no study to date has demonstrated any need to eradicate Clamydia or Mycoplasma to attain resolution of the salpingitis. High doses of one broad spectrum drug alone, such as Ampicillin, or a combination with broad spectrum, such as a penicillin with an aminoglycoside, almost always is adequate. In the event of Bacteroides being cultured from the peritoneal aspirate and lack of adequate clinical response, then a change of antibiotics to cover Bacteroides is indicated.

One recent disturbing development has been the appearance of a penicillin resistant gonorrhea. Over the years, Neisseria gonorrheae has become more resistant to penicillin by mutations of its D N A. The mechanism appears to be mainly decreased permeability of the organism to penicillin and other antibiotics. Thus, over the years, higher doses of penicillin were still effective. The new resistant gonococcus has acquired an "R factor" which codes for the enzyme penicillinase (B lactamase) and makes the penicillins completely useless. This strain is thought to have originated in the Far East, but is now worldwide. About 70% of these new resistant gonococci can be eradicated by the tetracyclines, but the treatment of choice is Spectinomycin 2 grams I.M. in one dose for uncomplicated gonorrhea.[16,22] No therapeutic guidelines are yet available for this penicillin resistant gonococcus when it is involved in salpingitis.

As we come to understand the bacteriology and pathogenesis of pelvic inflammatory disease better, we are modifying our approach to its treatment. The concept of treating only the gonococcus is giving way to a broader plan of attack. We now feel that coverage of the common secondary invaders such as the aerobic streptococci, peptococcus, peptostreptococcus, E. coli, and Bacteroides is desirable. Just what organism, combination of organisms, or change in

genital ecology initiates the ascent of infection is still poorly understood. Eradicating the gonococcus during the primary stage of infection in the cervix will certainly prevent some cases of salpingitis. As other organisms responsible for initiating the disease become identified, perhaps screening and then appropriate treatment of the carrier state of these organisms will reduce the incidence of this disease. But until that time, pelvic inflammatory disease will remain a common problem, and will become more difficult to treat as the penicillinase producing gonococcus becomes more prevalent.

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CHANGES — BELIEVE ME, I'VE SEEN SOME — *Continued from Page 308*

syringes, gloves and many, many other items.

About ten years ago, the decision was made that as experienced nurses we could do vaginal exams. After proper instruction and an observation period, we were permitted to do this procedure. This was a lot more comfortable for the patient, as most women will testify.

Also, about this time we started hearing that in some hospitals, husbands were allowed to be with their wives throughout labor and delivery. HEAVEN FORBID!! After a great deal of soul searching, attending classes with Mrs. Bing, and having patients pressuring us, we decided, with much trepidation, to accept and participate in this program. Today, Lamaze is highly skillful and is an accepted method of Childbirth Education, with nearly 85% of our deliveries accomplished by this method.

At the time of delivery, the baby is now placed in a KDC Infant Warmer, in the delivery room, and both Mother and Dad are encouraged to touch and hold the child. Then, Mother, if she wishes, has the opportunity to breast feed the baby on the delivery room table.

The next change that comes to mind is the introduction of the Fetal Monitor. This is one of the greatest steps toward the improvement in Intrapartal care. As nurses we apply Scalp Electrodes, and, with continual monitoring of the Fetal Heart Tones and uterine contractions, we can assure the patient and her husband that their baby is receiving the best care possible.

Induction of labor is now accomplished through the use of a dilute intravenous solution of Pitocin administered through an IVAC Pump. This pump accurately measures the dosage unit. Since the institution of this method of administration of Pitocin, and, the use of continuous fetal monitoring, I feel that the induction of labor, when indicated, is safer now than any other time in history.

I am very fortunate to have been associated with the nurses, physicians and other personnel throughout these twenty-odd years. I am also very fortunate to have been associated with such a progressive hospital as the Maine Medical Center.

As we enter the era of Perinatology, OB nursing is more challenging than ever, with the great strides being taken forward in prenatal care.

I may be one of "The Old Guard," but, I am very excited and eager to have an active role in this CHANGE.

Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The Maine Medical Association's House of Delegates, at its June 1976 meeting, adopted a regulation stating that a *minimum of 150* hours of continuing medical education is required in order to maintain membership. The policy took effect on January 1, 1977 and all members must be certified by January 1, 1980. Eligibility for certification begins January 1, 1977.

Credits required for the three-year period are as follows:

Category 1 — CME Activities with Accredited Sponsorship **(60 hours required)**	**No limit**
Category 2 — CME Activities with Non-accredited Sponsorship	**45 hours**
Category 3 — Medical Teaching	**45 hours**
Category 4 — Papers, Publications, Book and Exhibits	**40 hours**
Category 5 — Non-supervised individual CME Activities	**45 hours**
Category 6 — Other Meritorious Learning Experience	**45 hours**

Only active, dues-paying members are required to report. Please fill in your activity report promptly and return to the M.M.A. office, P. O. Box 250, Brunswick, Maine 04011.

The Hazards of Cigarette Smoking During Pregnancy

John J. Witte, M.D.

Recent national surveys indicate that in the last 20 years, women are taking up smoking in larger numbers and beginning to smoke at an earlier age.[1] "You've come a long way baby" is a sad, but true, comment on the smoking behavior of women in the United States. Women are now more vulnerable to the well-established smoking-related diseases, including lung and other cancers, myocardial infarction, bronchitis, and emphysema. In addition, women who smoke during pregnancy expose both themselves and their developing offspring to a variety of health risks.

The risks associated with cigarette smoking during pregnancy include lower-birth weight infants, increased perinatal mortality, greater incidence of abruptio placenta and placenta previa, and impairment of physical and intellectual development. Many of these untoward effects *are reversible,* provided the woman *stops smoking* by the fourth month of pregnancy.

Smoking and Birthweight

By the early 1970's, there was sufficient evidence to affirm a casual association between cigarette smoking and fetal growth retardation.[2] Smokers' babies generally weight 150 to 250 grams less than nonsmokers' babies. Women who smoke have twice the risk of having an infant that weighs less than 2500 grams. There is a strong dose-response relationship, with diminution in birth weight being directly proportional to the number of cigarettes smoked per day. These data are remarkably consistent in studies from many different countries, races, cultures, and geographic settings.

Smoking and Perinatal Mortality

There is a well-established, probably causal, association between cigarette smoking and higher late fetal and infant mortality rates.[2] A number of epidemiologic studies, both prospective and retrospective, show a statistically significant relationship between cigarette smoking and elevated mortality risks among offspring of smoking mothers. A series of articles by Meyer, et al[3,4,5] analyzed data from the Ontario Perinatal Study of all single births in 10 Ontario teaching hospitals in 1960-61. The study involved 51,490 births, including 701 fetal deaths and 655 early neonatal deaths. The risks for perinatal mortality among smoking mothers were shown to be greater among those women who already have other factors present which in themselves have an independent risk for elevated perinatal mortality. These include such factors as parity, socioeconomic status, previous pregnancy history, hemoglobin levels, etc. In addition, heavy smokers appear to be at greater risk than light smokers. Thus, the increase in risk for perinatal mortality associated with light smoking among young, middle or upper class, low-parity, non-anemic mothers is relatively low (about 10 percent). In contrast, women of high parity, low socioeconomic status, with previous low birthweight infants, or with hemoglobin levels less than 11 grams have rates of 70 to 100 percent higher than those for nonsmokers, depending on the amount smoked. Clearly, women who already have an elevated risk should be encouraged and assisted, where possible, by their clinicians to stop smoking.

Other Morbidity During Pregnancy

In addition to increased perinatal mortality rates among cigarette smokers, there is also an increased risk of placenta previa, abruptio placenta, bleeding during pregnancy, and prolonged rupture of the membranes among women who smoke cigarettes.[3,4,5] These conditions can affect the welfare of the mother as well as that of the infant. The level of risk for each of these problems is also dose related (i.e., higher risks among heavier smokers). Risks for both placenta previa and abruptio placenta are higher for smokers than for nonsmokers at all stages of gestation but appear to be slightly larger in the earlier weeks of pregnancy.

These conditions are likely due to the fact that cigarette smoke is directly related to arterial damage. Carbon monoxide (CO) is a component of cigarette smoke and results in elevated carboxyhemoglobin (COHb) levels in both the mother and fetus. A British study shows that after smoking a single cigarette, pregnant women have greater increases in COHb concentration than non-pregnant women.[6] In addition, fetal COHb levels are even higher than maternal levels, regardless of whether or not the mother smokes cigarettes. Studies with animals further support the association between significant exposure to CO and arterial damage. The increased exposure to CO in smokers is the likely mechanism of action for these conditions; however, this remains to be documented.

Long-term Effects on Physical and Intellectual Development

Several studies from the United States and Great

Continued on Page 316

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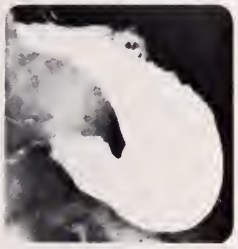

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†See Warnings, Precautions and Adverse Reactions.

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King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964

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THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.
For use in the treatment of infant colic (syrup).
Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS: Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis. WARNINGS: In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. PRECAUTIONS: Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with: autonomic neuropathy; hepatic or renal disease; ulcerative colitis—Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon, hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension; hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.
It should be noted that the use of anticholinergic/antispasmodic drugs in the treatment of gastric ulcer may produce a delay in gastric emptying time and may complicate such therapy (antral stasis). Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur. ADVERSE REACTIONS: Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia, urinary hesitancy and retention; blurred vision and tachycardia, palpitations, mydriasis, cycloplegia; increased ocular tension, loss of taste, headache, nervousness, drowsiness; weakness; dizziness, insomnia; nausea, vomiting, impotence; suppression of lactation, constipation, bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis, urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. DOSAGE AND ADMINISTRATION: Dosage must be adjusted to individual patient's needs.
Usual Dosage: Bentyl 10 mg. capsule and syrup: *Adults*: 1 or 2 capsules or teaspoonfuls syrup three or four times daily. *Children*: 1 capsule or teaspoonful syrup three or four times daily. *Infants*: ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 20 mg.: *Adults*: 1 tablet three or four times daily. Bentyl Injection: *Adults*: 2 ml. (20 mg.) every four to six hours intramuscularly only. NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE: The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine® (bethanecol chloride USP) should be used.
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Britain demonstrate an association between smoking in pregnancy and impaired physical and intellectual development in the offspring.[7,8,9,10]. One large study found statistically significant differences in height and reading ability at 7 and 11 years of age; depending on whether or not mothers smoked during pregnancy.[7]

Physicians and other professional persons working with pregnant women who smoke have an obligation to help them stop smoking at least for the duration of their pregnancy. Optimally, doctors should set an example and not smoke. For those who continue to smoke, however, (approximately 20 percent), it is strongly recommended that they not do so in the presence of their patients. Similarly, nurses and others working in physicians' offices, clinics, and hospitals should not smoke in patient areas. Smoking should be prohibited in these areas.

The use of posters or brochures in the patient waiting areas is often helpful, as well as informative, and can facilitate the physician-patient dialogue on smoking. Brochures and posters can be obtained from local offices of the American Cancer Society and the American Lung Association.

Many pregnant women are not aware of the increase in risks involved as a result of their smoking. They should be made aware of the unique health hazards, both to themselves and to the developing fetus, and they should be urged to quit. Adequate information to make a decision and a professional recommendation toward the proper decision are necessary steps, even if the patient is not able to successfully stop smoking. Many women are concerned about weight gain after quitting. Although some weight gain may follow, this is generally not a major problem for most people.

There are no gimmicks, gadgets, techniques, or approaches that are universally successful to help the smoker quit. For most habituated smokers, tapering off will not facilitate the quitting process. The smoker needs to make a personal commitment to stop and needs to set a date to do so. Stopping "cold turkey" is very difficult for most people. Encouragement and reinforcement are helpful in the first few days and weeks after quitting. Such encouragement should come from the patient's family and friends as well as the physician and members of the office staff. During the early days and weeks (after quitting), it is helpful to provide an environment free from smoke and smokers.

Those people not able to quit on their own can be referred to smoking cessation clinics run by the major voluntary agencies for free help or to commercial groups that conduct cessation programs. The rates of success of these groups vary, but average about 30 percent success rates, as measured by persons who are not smoking one year later. They rely largely on group dynamics, helpful tips from successful "quitters," and a mutual desire to stop smoking.

Since the consequences of smoking in pregnancy

Continued on Page 320

A Review of the Management of Twin Gestation

GREGORY LUCK, M.D.* AND C. IRVING MEEKER, M.D., F.A.C.O.G.**

ABSTRACT

A review of the literature was conducted regarding the management of twin gestation. Both antepartum and intrapartum problems are discussed. The available data suggest that cesarean section should be used more liberally in twins, especially if the presentations are anything other than vertex/vertex.

INTRODUCTION

The incidence of twin gestation varies from paper to paper but most authors agree that twinning occurs with an overall average of 1/90 pregnancies.[1,4,5,16] Monozygotic (MZ) twins are reported in one out of every 250 pregnancies. This figure is relatively constant throughout the world.[1,16] The incidence of dizygotic (DZ) twins varies with many factors including race, geographic location and socioeconomic status. The frequency appears to increase with age, parity, elevated endogenous gonadotropin levels, the use of infertility agents, and with a maternal history of twins.[1,4,5,16]

Dizygotic twins are the result of fertilization of two separate ova. By contrast MZ twins develop when a single fertilized ovum divides at an early stage. Each of the resulting cell clusters has the potential for full development. With DZ twins, there are two separate placentas and sets of membranes, although they may appear fused. The placentas formed in MZ pregnancies may be diamniotic dichorionic, diamniotic monochorionic, or monoamniotic monochorionic depending on the time of division.[16]

DIAGNOSIS

The antepartum diagnosis of twins has always been difficult. Less than 50% are diagnosed prior to the onset of labor and in some reports, this has been as low as 5%.[1,2,4,5,8] It is important to make the diagnosis early in order to try and prevent premature delivery. The diagnosis is made by history, physical examine and laboratory data. The most important historical data leading to a suspicion of twins would be the prior use of fertility agents. A positive family history of twins is also important.[2,16] The presence of a uterus that is large for dates is the major physical finding of importance. A difference of more than 4cm. between the gestational age and the fundal height, using the MacDonald measurement, has been reported as strongly suspicious of twins. This applies between 22-34 weeks gestation.[2] The identification of two fetal hearts is more certain but there should be a difference of at least 10 beats per minute on simultaneous examination.[1,16] The most common method of diagnosis today is by ultrasound or x-ray. A distinct gestational sac may be identified by sonography as early as 6 weeks gestation. The fetal skull can be identified by 14 weeks gestation.[1,2,4,16] Screening biochemical tests such as HCG levels have not proved satisfactory.[9,3] However, elevated serum alpha fetoprotein levels, found in mass screening programs, have been associated with twins and may prove more useful.[1] Twin gestation should also be suspected with unexplained anemia, or widening transverse abdominal diameter during pregnancy. Mile pre-eclampsia during the last trimester of pregnancy is more common with twin gestations and may be an early clue to the diagnosis.[1,2]

The early diagnosis of twins is improving. In a Scandinavian study, only 16% of twins were diagnosed prior to 32 weeks gestation between 1965-1970. Between 1971 and 1973, the rate of early diagnosis had jumped to 40%.[8]

TWINS AS HIGH RISK PREGNANCY

The perinatal mortality rate for twins varies from 5 to 20% in different studies. However, most authors agree on a 10 to 15% mortality rate.[1,2,4,5,6,10,16] The marked increase in perinatal mortality is largely related to a combination of premature delivery and intrauterine growth retardation (IUGR).[2] Both of these complications are seen more often with twin B.[5,16] Premature delivery at less than 37 weeks occurs in 50% of twin pregnancies.[5] Mortality rates compared to gestational age are reported in the following table.[5]

Gestational Age[5]	*Mortality Rate*
Less than 30 weeks	59%
30-33 weeks	27%
34-37 weeks	8%
greater than 37 weeks	4%

The intrauterine growth of each twin is comparable to that of a singleton up to 30-32 weeks gestation. After that, the combined weight gain may be nearly the same as that for a single fetus due to the relative placental insufficiency which occurs. The biparietal diameters, however, increase proportionately to gestational age due to the "brain sparing" mechanism, unless severe IUGR takes place.[1] A comparison of birth weights with mortality in twins is

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shown below.[5]

Birth Weight (GMS)	*Total Death Rate*
Less than 500	100%
500-1000	81%
1001-1500	43%
1501-2000	9.2%
2001-2500	4.7%
Greater than 2500	0%

Various series show 45%-60% of twins have birth weights less than 2500g. As many as 50% of those carried to term weigh less than 2500g.[5] However, in one study, the mortality rate for twins by weight was found to be the same as that for singletons. This implies that in addition to prematurity, IUGR plays a significant role in increasing the perinatal mortality.[5]

Other problems associated with twinning include a higher rate of abortion, hypertensive disease of pregnancy, hydramnios, and premature rupture of the membranes. With monochorionic placentas, there are often vascular anastomoses, some of which are significant enough to cause disparity in fetal size, or worse, a fetal transfusion syndrome. In the latter, congestive heart failure, hydramnios, polycythemia and severe hyperbilirubinemia can develop in the recipient. Congenital heart disease, other anomalies or fetus papraceus and subsequent DIC can occur in the donor.[1,2,4,5,6,16] With monoamniotic placentas, a 50% mortality rate is observed 2° cord complications and conjoined twins.[4] For unexplained reasons, monozygotic twins have 3 times the perinatal mortality compared to dizygotic twins.[5]

At the time of labor an increased incidence of malpresentations is seen. A 17% incidence of breech presentation in twin A and a 41% incidence of breech in twin B has been reported.[6] One large review showed a 3-5 fold increase in perinatal mortality in vaginal breech delivery of twins for both twin A or twin B.[5] In another study, an increased incidence of mid-forcep deliveries (8.8%) was reported.[6] Ho and Wu from USC reported that the cesarean section rate was twice as high for twins as for singletons. They found that this reduced the overall neonatal mortality rate from 6.23% to 1.45% within their own experience. The same study showed a consistently lower apgar score for twin B especially when twin B was delivered vaginally as a breech.[6] Special care nursery admission is required for up to 59% of neonatal twins. Other frequent problems encountered in the neonatal period include hypoglycemia, hypocalcemia and hyperbilirubinemia.[6]

Prenatal Management

Once the patient has been identified as carrying twins, there are a few basic changes in prenatal management that should occur. Caloric intake should be increased by 300 Kcal/day and protein intake by 1.5g/kg day. Supplemental iron and vitamins, especially folic acid, should be added.[16] Abdominal support garments should be used as needed for patient comfort. The patient should be followed closely for appropriate weight gain and the development of hypertension, hydramnios, anemia or premature cervical dilation.[1,4,14] Because significant differences in growth rates can occur, development must be followed carefully and is best accomplished by serial ultrasound examination every four weeks. These shoud be obtained even more frequently if some disparity in growth occurs. In one study, a 2 to 6mm difference in biparietal diameters was associated with a 40% incidence of low birth weight (LBW) in the smaller infant. With a greater than 6mm difference in biparietal diameters, the incidence of LBW increased to 71%.[12] It is suggested that head/abdominal ratios be used as a more accurate method of assessment of fetal growth.[1] If intrauterine death occurs, weekly DIC screens should be performed and the remaining pregnancy should be terminated if a coagulation defect begins to develop.[1,4]

In the absence of a previous diagnosis of incompetent cervix, circlage has not been effective as a method treatment of premature dilatation of the cervix.[15] However, there are centers including the New York Lying In Hospital, that have tried this approach to prevent premature cervical dilatation.[4] When a history of incompetent cervix is obtained, circlage should be performed early in the second trimester.[4]

Bed rest has been recommended as a major factor in the prenatal management of twins. The usefulness of this, however, has not been satisfactorily demonstrated.[15] The rationale for bed rest in the lateral position is to avoid the inferior vena cava syndrome, increase uterine blood flow, and reduce pressure on the cervix. At Yale, this treatment is instituted only if differential growth rates are identified, if hydraminos is documented by sonography or if silent cervical dilatation is noted.[1] Other centers use limited activity and bed rest only if problems arise.[4]

If premature labor occurs, tocolysis is attempted in most centers before 37 weeks unless contraindicated on obstetrical grounds.[2,4,16] Cortisteroids are recommended if premature labor occurs before 32-34 weeks gestation.[2]

Finally, if prematurity is likely and an L/S ratio is indicated, several papers have shown that the L/S ratios in both sacs are the same unless one infant is relatively growth retarded and stressed. In this case two taps are recommended. One half cc of indigo carmen is instilled as a marker in the first sac so that both sacs are actually tested.[1,12] If only a single tap is performed, then a ratio of 2.5/1 should be used to indicate maturity thus allowing an extra margin of safety for the second fetus.[12]

Management of Twin Labor and Delivery

At the onset of labor, a KUB should be obtained to ascertain the position of both *fetuses*. One study found only 7% were vertex/vertex with other compound presentations the rest of the time.[5] In 1973,

Farooqui reported a 3 to 5 fold increase in perinatal mortality associated with the vaginal delivery of a breech presentation for both twin A and twin B. The rates for other compound presentations were even higher.[5] Another study, from USC, in 1975, reported consistently lower apgar scores for twin B. The scores were worse if twin B was in a breech presentation. They also reported lower apgar scores for twin A if it was a breech as compared with a vertex presentation. The same study showed a marked decrease in perinatal mortality for all presentations if cesarean section was performed.[6] This data suggests that the appropriate management for a twin pregnancy with anything but a vertex/vertex presentation would be delivery by cesarean section. This is certainly not standard practice at present.

If vaginal delivery is chosen and labor is allowed to continue, it is generally suggested that both twins be monitored, although available data have not yet shown a decreased perinatal mortality rate associated with the continuous monitoring of both twins.[1,2,6] Pressure tracings can be obtained on both monitors by making the appropriate connections between the two pressure transducers and the single intrauterine catheter.[11] Two units of blood should be typed and crossmatched and a large bore intravenous line started.[16] With appropriate monitoring, Pitocin® augmentation has been carried out with no increase in morbidity or perinatal mortality.[4]

Adequate personnel should be available for delivery.[16] Analgesia and anesthesia should be held to a minimum due to the large number of premature twins.[16] Pudendal block is the preferred method of anesthesia with supplemental nitrous oxide as back up.[16] In one study, this method was associated with a decreased perinatal mortality as compared with all other methods of anesthesia.[4] Delivery management for twin A is the same as it would be for a single fetus. The cord is cut and clamped but blood is not collected at this time because of the rare possibility of a vascular anastomosis with twin B. Following the delivery of twin A, the presentation of twin B and its relation to the pelvic inlet is established.[16] There is still some controversy regarding the delay between deliveries. It is important to keep the time between delivery of the infants as short as possible in order to reduce perinatal mortality and maternal morbidity. Most authors agree that if no active contractions have resumed within 10 minutes, augmentaion with Pitocin is warranted.[2,4,16] Amniotomy is performed and an electrode applied to the presenting part as soon as engagement is accomplished. With vertex presentations and with most breech presentations from this point on the delivery, management is similar to what it would be for a singleton delivery. If the breech or vertex does not immediately present at the inlet and version extraction is considered, this should be carried out immediately least uterine tone return.[4,16] If this procedure is performed at this time, no anesthesia or only light anesthesia with nitrous oxide, O_2 and Penthrane® should be necessary. If the uterus contracts, brief halothane anesthesia can be used for uterine relaxation.[4,16]. If twin B is felt to be much larger of if version extraction attempts are unsuccessful, prompt cesarean section should be undertaken.[9,16] Because of this possible need for immediate cesarean section, twins should usually be delivered in an operative delivery room. Expert care must continue in the 3rd stage because of the increased incidence of post partum hemorrhage, especially after halothane relaxation. Unless prompt spontaneous delivery of the placenta occurs, manual removal and exploration for retained parts and uterine defects has been recommended followed by bimanual massage and an IV Pitocin drip.[4,16]

Conclusion

1. Diagnosis: A high index of suspicion, the increased use of routine sonography and perhaps routine screening for AFP should improve the early diagnosis of twins.

2. Prenatal Management: Serial sonograms for fetal growth are suggested. Bed rest is not routinely required but is probably indicated if

   a. There is increasing disparity in fetal size as seen on serial sonograms.
   b. hydramnios occurs or
   c. premature dilatation of the cervix is found through serial vaginal exams.

Vaginal delivery is usually appropriate with any vertex/vertex presentation. Cesarean section should be considered for any other combination of presentations. If vaginal delivery is elected with either fetus in the breech presentation, the delivery is best done in an operating delivery room, where an emergency cesarean section could be carried out if necessary.

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THE HAZARDS OF CIGARETTE SMOKING DURING PREGNANCY

Continued from Page 316

are all dosage related, those who are unable or unwilling to stop entirely should be advised to reduce their dosage. This can be accomplished by the following: (1) smoke fewer cigarettes each day, (2) select a low "tar" and nicotine brand, (3) take fewer puffs of each cigarette smoked, and (4) do not inhale each puff as deeply. There are commercial devices on the market (for example, Water-Pik) designed to reduce the level of "tar" and nicotine; however, any advertised claims toward facilitated cessation of smoking are not substantiated by firm facts.

In summary, the risks of smoking during pregnancy are significant and well documented. Physicians are obliged to educate their patients about these risks and do whatever they can to aid them in quitting.

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MEASLES

This past spring a measles epidemic of at least 1300 cases occurred in Maine. Many areas of the state were not affected and it is anticipated that another epidemic will occur this school year.

In the past, measles was a disease of pre-schoolers and elementary school students, but in the past few years a majority of cases nationwide have been among teenagers. This pattern was evident in Maine this past school year as 60% of the cases occurred in children 10 and older.

The reason for this change in age distribution of measles is that there is a large pool of susceptibles among Junior and Senior High students. Two circumstances combined to produce this situation. The measles vaccines used prior to 1968 were either killed virus or live virus combined with gamma globulin. The immunity provided was short-lived. The exception to this was the Edmonston B measles vaccine, which still provides immunity even if combined with gamma globulin. Secondly, since measles has been relatively uncommon in the past decade and hence the present Junior and Senior High students have had little contact with measles.

In order to avert another measles epidemic this school year, we urge physicians to vaccinate all their teenager patients who were vaccinated prior to 1968 or before their 1st birthday. The exceptions to this would be: 1) teenagers, who the physician knows have had measles, 2) those vaccinated since 1968, or 3) those who received Edmonston B vaccine.

The Department of Human Services is organizing a measles vaccination campaign this fall in Junior and Senior High Schools and needs the cooperation of Maine's physicians. We urge you to vaccinate your young patients and to support these clinics.

STEFAN ZINESKI, M.D.
State Epidemiologist

Pelvimetry and Active Management of Labor

CLAUDIO DELISE, M.D.* AND DONALD MCCRANN, M.D., F.A.C.O.G.**

ABSTRACT

X-ray pelvimetry in the management of dysfunctional vertex labor is probably of no value. Pitocin® augmentation should be followed by direct fetal monitoring and intrauterine pressure catheters. Cephalopelvic disproportion should be diagnosed only after adequate dilatation has taken place and the presenting part has failed to descend with documented adequate uterine forces.

At the Maine Medical Center, 50% of primary cesarean sections are performed for failure to progress, failure to dilate, cervical dystocia, and cephalopelvic disproportion. The distinction between these diagnoses is not always clear by examining the patient's record. Failure to progress, failure to dilate, certival dystocia should not as a rule be indications for cesarean section.

INTRODUCTION

Pelvimetry was introduced in the 1930's, and quickly became accepted in obstetrical practice and continues to be used in the management of labor. Presently pelvimetry accounts for over 72% of the x-ray exams in pregnancy,[1] and with the ultrasound examination replacing x-ray for determination of fetal age, fetal position and placental localization, this percentage is increasing. While the published literature on risks of x-ray radiation is equivocal, there is at least a theoretical risk to the fetus exposed to pelvimetry.[2,3] In order to offset this potential risk, a diagnostic tool should be of proven value in reducing morbidity and mortality in labor.

Kelly, et al[1] reviewed 67,078 deliveries of greater than 1000 gm birth weight. This involved 16 hospitals and 4,599 pelvimetries (6.9%). These authors found no correlation between the cesarean section rate at each hospital and the use of pelvimetry which varied from 1.8% to 15.7%. They also found pelvimetry was not prognostic of route of delivery since with normal pelvimetry, 27% still resulted in a cesarean section.

In general, pelvimetry was not able to shorten labor by identifying cases of cephalopelvic disproportion. In fact, patients with normal pelvimetry who failed a trial of Pitocin induction, had an additional two hours of labor as compared with a group that failed augmentation without x-ray pelvimetry.

Russell and Richards[4] examined 833 cases of pelvimetry and compared them to 110 controls who were referred for x-ray assessment of fetal maturity. They found pelvic size of the two groups not to be statistically different. Assessing the mean weight in the pelvimetry group they found no differences between vaginal or abdominal deliveries. In fact, the mean weight in the pelvimetry group of 3.2 kg was less than the 3.4 kg mean birth weight found in a random sample of all deliveries at their hospital.

The pelvimetry group had a section rate of 29%, and a forceps delivery rate of 27% as compared to the 8.4% overall hospital forceps rate. It thus appears from both studies that the patients selected for pelvimetry are those that have abnormal labor patterns but not necessarily those with small pelves.

To determine what the incidence of cephalopelvic disproportion is in a normal population, O'Driscoll, et al[5,6] studied 1000 consecutive primiparas prospectively. Their hospital had switched to active management of labor a few years before.[5] This implied that if a patient in labor showed any deviation from normal progress, membranes were ruptured and if this had no effect, labor was augmented with Pitocin. All but one were delivered in less than 24 hours. Active management was used in roughly 20%. Fetal morbidity and mortality in the period of 1966 to 1968 was significantly lower compared with a similar sample in 1963 to 1965, when a more conservative approach was used. The primary cesarean section rate for all cases in this study was 4%. Cephalopelvic disproportion was suspected in 30 cases (3%) because of an unengaged head in labor. The final diagnosis of cephalopelvic disproportion was made in 9 out of 1000 patients (0.9%).

THE MAINE MEDICAL CENTER EXPERIENCE

At Maine Medical Center, for the year 1977, the primary cesarean section rate was 15.7% and although most observers would attribute this high rate to the advent of fetal monitors, this is not borne out by individual cesarean section chart review. Only 2% of the total deliveries were sectioned for fetal distress. Seven percent were sectioned for cephalopelvic disproportion, failure to progress, arrest of labor, cervical dystocia, etc. The remaining 6.7% were due to malpresentations and maternal indications. Fifty percent of all the primiparous sections were for cephalopelvic disproportion and associated problems of labor. In the analysis of the cesarean section rate of individual members of the obstetrical staff at Maine Medical Center, one notices a wide variation in their overall section rate and their section rate for cephalopelvic disproportion (see Table 1). Interestingly, physician #1 and #2 rely strongly on x-ray pelvimetry, while physician #10, 11, 12, and 13 seldom, if ever, use x-ray pelvimetry in labor

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TABLE 1

STATISTICS FOR 1977 FOR STAFF PHYSICIANS AT MAINE MEDICAL CENTER

M.M.C. Staff Physician	*C.P.D. C. Section Rate (%)*	*Primary C/S Rate (%)*
1	13.6	20.5
2	12.5	25.0
3	11.4	21.3
4	9.4	25.9
5	9.1	15.8
6	8.3	16.7
7	7.5	23.3
8	7.1	17.1
9	6.5	15.2
10	5.3	19.5
11	5.1	5.1
12	4.2	7.0
13	0.	5.2

management. But since #8 and #9 use pelvimetry and #4 never does, the graph does not necessarily show a higher section rate for pelvimetry users.

The wide variation in section rates would imply that at least some of the patients might have delivered vaginally if managed differently. Many of the patients whose records were reviewed were sectioned with cervical dilatation less than 4 cm. Since, in general, descent follows cervical dilatation, which follows cervical effacement, it is suggested that many of the patients were sectioned before arrest of descent could be documented; more a case of cephalocervical disproportion than cephalopelvic disproportion.

DISCUSSION

According to Friedman,[7] the latent stage of normal labor may be as much as 20 hours in a primipara and 14 hours in a multipara. Since in augmentation, one is attempting to change a dysfunctional labor pattern to normal, it does not follow that a patient should be sectioned for failing to progress at rates that one would consider rapid even for normal labor. Latent phase is, by its nature, slow because the energy generated by the uterine contractions is expended to develop the lower uterine segment, and to efface the cervix prior to dilatation of the cervix. The mechanism of dilatation is relatively independent of pelvic size. Dilatation many times will proceed to 9-10cm. even in obvious cephalopelvic disproportion where the vertex fails to engage in a contracted inlet.

What we then suggest as a method to reduce the increasing section rate is to give all patients in dysfunctional labor a trial of Pitocin, to identify true cephalopelvic disproportion. This should be done with definite guidelines to avoid maternal or fetal injury.

In the previously mentioned study by O'Driscoll, electronic fetal monitoring was not used routinely. That may have been standard practice in 1968, in the British Isles, but in 1978, a potential cephalopelvic disproportion patient should be considered high

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risk and should be monitored. Furthermore, to be able to augment a patient safely, intrauterine pressure monitoring should be used. Without this technique, one may inadvertently exceed safe uterine pressures which may harm the fetus by wedging the head into a borderline tight pelvis, making for a very difficult and traumatic cesarean section. Also, without internal pressure monitoring, one may be lulled into believing that contractions are adequate on the basis of patient's subjective discomfort or palpation of contraction strength. This would lead to prolonged inadequate Pitocin use. By actually measuring intrauterine pressures, I.V. Pitocin doses can be safety titrated for maximum effect with the use of IVAC or Harvard constant infusion pumps.

The diagnosis of cephalopelvic disproportion is made by the failure of the head to pass through the pelvis with a driving force comparable to the force found in normal labor.

This descent through the birth canal should not be protracted (barring an OP presentation) since this would strongly suggest relative C.P.D.

There is no question that with prolonged use of oxytocin a fetus may be driven deep enough in the pelvis to tempt the operator to try a midforcep delivery. Friedman[8,9] has shown statistically that this combination of abnormal labor pattern with a midforcep operation has an unacceptably high rate of fetal morbidity and mortality.

While this paper will not solve the problem of how to deliver the patient with abnormal labor pattern, we must keep in mind that cesarean section has a significant increase in maternal morbidity and mortality. Evrard and Gold [10] reviewed the Rhode Island experience for 1965-1975 and found the maternal mortality rate to be 6.95/10,000 as compared to 0.27/10,000 for vaginal deliveries. This amounts to a 26 times greater mortality risk.

This type of active management of the abnormal labor pattern is not recommended as a universal approach. Prerequisites include knowledge and application of the normal and abnormal Friedman labor curves, continuous electronic fetal monitoring, constant infusion pumps for intravenous oxytocin augmentation, and the capability for rapid cesarean section. Careful clinical exam of the pelvis and presenting part, as well as x-ray if a malpresentation is suspected is essential before augmentation of labor.

The goal of this type of approach is not to deliver all babies vaginally but to allow those with an abnormal labor curve a trial of carefully monitored oxytocin for a reasonable time period to make the diagnosis of cephalopelvic disproportion.

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Fall Meeting of the M.M.A. House of Delegates

Saturday, December 9, 1978

Mid-Maine Medical Center (Thayer Unit), Waterville, Maine

12:30 P.M.—Registration; 1:00 P.M.—Lunch; 2:00 P.M.—Meeting

10:00 A.M.—Meeting of the Executive Committee

NEW HOSPITAL AGREEMENT NEGOTIATED

Incentives to contain hospital costs will be provided through a new Blue Cross Participating Hospital Agreement (contract) negotiated by the Maine Hospital Association (MHA) and Blue Cross and Blue Shield of Maine.

The new hospital contract, which was ratified after lengthy negotiations by a majority of the MHA member hospitals and the Board of Directors of Blue Cross and Blue Shield of Maine, offers specific reimbursement incentives to those member hospitals which contain their costs by some of the following methods:

—Voluntarily limiting its increase in per diem costs to an average maximum of approximately 12% per year over a *three year* period (this increase is well below the current trend based on Blue Cross cost reports).

—Voluntarily reducing its licensed bed capacity in order to reach certain occupancy level percentages (ranging from 70-90%). Excess hospital beds are generally believed to be one of the prime elements in escalating hospital costs, since an unoccupied bed still costs 65% (or more) as much to maintain as an occupied bed.

—Maintaining the same ratio of full time hospital employees per patient as in the previous fiscal year. Personnel costs are a major factor in hospital budgets and have increased sharply in recent years. Limiting the employee/patient ratio should help hold the line on personnel costs.

—Funding depreciation. By setting aside a sum that could be used to replace buildings and equipment, the hospital would not have to borrow for such purposes. In recent years, the rate for long-term indebtedness of hospitals has increased substantially with a corresponding effect on per diem costs.

The new contract continues to support the Certificate of Need Act, whereby hospitals must submit plans for facility expansions/replacement and costly equipment purchases to the State Department of Human Services and the Maine Health Systems Agency for approval.

Although the new participating agreement may initially result in slightly higher payments to hospitals already qualifying under the incentive programs, it is believed that these same incentives will induce many more hospitals to implement programs which will reduce the future rate of escalation in costs.

he was chief of obstetrics and gynecology for many years.

Surviving are his widow, the former Doris L. Dyer; and a sister, Mrs. Edgar Hagen of Portland.

EDWARD L. CURRAN, M.D.
1917-1978

Dr. Edward L. Curran, 61, of Bangor, Maine, died on June 12 in a local hospital following a long illness.

Born in Bangor, Maine on January 9, 1917, he was the son of Dennis F. and Grace L. Curran.

He was graduated from Bowdoin College and received his medical degree from Cornell University Medical College in 1942. He interned and served residencies at the Bellevue Hospital in New York.

Dr. Curran served in the U.S. Army during World War II. He located in Bangor in 1949 where he was a staff member of St. Joseph Hospital and a past president of the Eastern Maine Medical Center medical staff.

He was a member of the Penobscot County Medical Society and the Maine Medical Association. For many years, he was city physician and team physician for Bangor High School.

Surviving besides his mother of Bangor are his widow, Nellie Curran of Bangor; four sons, Edward L. Curran, Jr. of Brewer, Peter D. Curran of Bangor, Stephen A. Curran of Portland and Matthew J. Curran of Orono; three daughters, Mrs. Rosemary Tyson and Miss Theresa L. Curran, both of Kennebunkport, and Mrs. Margaret Fortier of Fairfield; one sister, Mrs. Christine Hillman of Bangor; and four grandchildren.

JOHN YOUNG, M.D.
1910-1978

Dr. John Young, 67, of Bethel, Maine, died in his home on June 15.

Born in Codroy, Newfoundland on November 24, 1910, he was the son of William and Deborah Young.

He attended Harvard University, was graduated from Johns Hopkins University and received his medical degree from Tufts University School of Medicine in 1939. Dr. Young interned at the Jersey City Medical Center. He practiced in Jonesport from 1942 until 1959, when he located in Bethel.

Dr. Young was a member of the Oxford County Medical Society, the Maine Medical Association, the American Medical Association and the American Academy of Family Practitioners and was a staff member of the Stephens Memorial Hospital in Norway.

Surviving are a daughter, Mrs. Carol Colby of Rumford; two sons, John of Colorado and Darrell of Bethel; a sister, Mrs. Hilda Kaminskus of Northampton, Massachusetts; and three grandchildren.

LEONARD G. MIRAGLIUOLO, M.D.
1905-1978

Dr. Leonard G. Miragliuolo, 72, of Bangor, Maine, died on July 14 in a local hospital.

Born in Ischia, Italy on July 18, 1905, he was the son of Nicola and Clementina Miragliuolo.

He was graduated from Providence College, received his medical degree from the University of Rome School of Medicine in 1937, interned at the Charles Chapin Hospital in Providence, Rhode Island and the Eastern Maine Medical Center in Bangor, and served a residency at the Eastern Maine Medical Center.

Dr. Miragliuolo located in Bangor in 1940 where he was on the medical staff at the Eastern Maine Medical Center and St. Joseph Hospital. During World War II, he served in the U.S. Army Medical Corps in Iran and India as a Major.

A senior member of the Penobscot County Medical Society and the Maine Medical Association, he was a past president of the Penobscot County Medical Society and served as Vice Speaker of the Maine Medical Association House of Delegates from 1971-1972. Dr. Miragliuolo was also a member of the American Medical Association, the American Academy of Family Physicians, the American Society of Abdominal Surgery, the New England Board of Obstetrics and Gynecology, the board of directors of Maine Blue Cross and Blue Shield for 17 years, and was past president of the medical staff at St. Joseph Hospital.

Surviving are his widow, Merle D. Miragliuolo of Bangor; four sons, Nicola J. of Nashua, New Hampshire, Leonardo D., Robert T. and Paul F., all of Bangor; three daughters, Mrs. Wallace Pieculewicz of Hudson, Massachusetts, Mrs. Hall Elliott of Bangor, Mrs. Douglas Wienzierl of Willimantic, Connecticut; one brother, Joseph Miragliuolo and one sister, Mrs. John Cicilline, both of Narragansett, Rhode Island; and four grandchildren.

MARGARET R. (SIMPSON) ZELTZERMAN, M.D.
1906-1978

Dr. Margaret R. (Simpson) Zeltzerman, 71, wife of Dr. Israel Zeltzerman, of Cape Elizabeth, Maine, died on July 30 in a Portland hospital following a brief illness.

Born in Scotland, Connecticut on October 16, 1906, she was the daughter of George and Ella Simpson.

She was graduated from Simmons College in Boston, Massachusetts and received her medical degree from Boston University School of Medicine in 1934.

For many years, she was affiliated with the Division of Mental Health at the Department of Health and Welfare in Augusta, Maine.

She was a senior member of the Kennebec County Medical Association, the Maine Medical Association and the American Medical Association.

Surviving is her husband of Cape Elizabeth.

J. ROBERT DOWNING, M.D.
1912-1978

Dr. J. Robert Downing, 66, of Kennebunk, Maine, died in his home on August 3 following a long illness.

He was born in Brighton, Massachusetts on May 17, 1912, the son of Jere R. and Georgia H. Downing.

A graduate of Duke University, he received his medical degree from Duke University School of Medicine in 1939, served an internship at the Maine General Hospital, and started his practice in Kennebunk in 1942.

During World War II, Dr. Downing served in the U.S. Army Medical Corps as a Lieutenant Colonel.

He was a member and past president of the York County Medical Society, a member of the Maine Medical Association, was on the staff of the Webber Hospital in Biddeford, and served as medical examiner for the State of Maine for many years. In 1971, the Kennebunk-Kennebunkport Chamber of Commerce selected Dr. Downing as one of the citizens of the year.

Surviving are his widow, Leta Marr Downing; two daughters, Mrs. Peter Morrison of Hanover, New Hampshire and Mrs. John Ouellette of Bradenton, Florida; a stepsister, Leota Langley of Clearwater, Florida; a stepbrother, Lawrence E. Langley of Nashua, New Hampshire; and three granddaughters.

MORRILL SHAPIRO, M.D.
1924-1978

Dr. Morrill Shapiro, 54, of Portland, Maine, died in a local hospital on August 14.

Born in Biddeford, Maine on June 24, 1924, he was the son of Samuel S. and Nettie Shapiro.

He was graduated from Bowdoin College and received his medical degree from Albany Medical College of Union University

in 1949. Following his internship and residency at the Maine General Hospital, he served in the U.S. Army Medical Corps in the Korean Conflict as a 1st Lieutenant.

Dr. Shapiro located in Portland in 1956 and was an active staff member of the Maine Medical Center, Mercy Hospital, Westbrook Community Hospital and Portland City Hospital. He was also chief medical officer for the Maine Central Railroad, H.P. Hood Company and the Central Maine Power Company, and was assistant clinical professor of Tufts University School of Medicine.

He was a member of the Cumberland County Medical Society and the Maine Medical Association, and was certified by the American Board of Surgery.

Surviving are his widow, Muriel Shapiro of Portland; two daughters, Mrs. Lynne Gordon of Far Rockaway, New York and Susan Shapiro of Brookline, Massachusetts; a son, Steven Shapiro of Portland; a brother, Irving of Lynn, Massachusetts; and two grandchildren.

Jacob Smith, M.D.
1908-1978

Dr. Jacob Smith, 69, of Bath, Maine, died in a local hospital on August 24 following a short illness.

Born in Brunswick, Maine on October 28, 1908, he was the son of Samuel and Mary Smith.

He was graduated from Bowdoin College and received his medical degree from the University of Vermont College of Medicine in 1935. Dr. Smith interned at the Auburn City Hospital in New York and in 1936 located in Bath.

During World War II, he served in the U.S. Army Medical Corps in the Pacific Theater and retired in 1946 as a Major.

Dr. Smith was an affiliate member of the Lincoln-Sagadahoc County Medical Society and the Maine Medical Association.

Surviving are his widow, Sara L. Smith of Bath; a son, Richard Smith of Woolwich; three sisters, Ida Young of North Windham; Sadye Chatman of Flint, Michigan and Fannie Simpson of Trenton, New Jersey; and a grandson.

Walter L. H. Hall, M.D.
1910-1978

Dr. Walter L.H. Hall, 67, of Old Town, Maine, died in a Bangor hospital on August 26.

Born in Orono, Maine on September 27, 1910, he was the son of Dr. Walter C. and Belle Hall.

He was graduated from the University of Maine and received his medical degree from Harvard Medical School in 1936. He served a three-year internship at the Knickerbocker Hospital in New York City and was a resident in surgery at Seton Hospital, also in New York City. Dr. Hall served in the U.S. Navy Medical Corps as a Lieutenant Commander in the Pacific Theater of Operations during World War II.

Dr. Hall located in Old Town in 1939. He was a member and past president of the medical staff at St. Joseph Hospital, and a member of the surgical staffs at Eastern Maine Medical Center and St. Joseph Hospital.

He was a member of the Penobscot County Medical Society, the Maine Medical Association and the American Academy of Family Physicians, and was certified by the American Board of Surgery.

Surviving are his widow, Clare Hall of Old Town; two sons, John E. Hall of Miami, Florida and Peter H. Hall of Old Town; and one grandson.

AMA Schedule of Meetings

ANNUAL CONVENTIONS
1979 July 22-26 Chicago
1980 July 20-24 Chicago

INTERIM MEETINGS — HOUSE OF DELEGATES
1978 December 3-6 Chicago
1979 December 2-5 Honolulu

Tablets
PERCOCET®-5 (II)

Brief Summary of Prescribing Information

DESCRIPTION Each tablet of PERCOCET®-5 contains 5 mg oxycodone hydrochloride (WARNING: May be habit forming), 325 mg acetaminophen (APAP).

INDICATIONS For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS Hypersensitivity to oxycodone or acetaminophen.

WARNINGS Drug Dependence Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of PERCOCET®-5, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, PERCOCET®-5 is subject to the Federal Controlled Substances Act.

Usage in ambulatory patients Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using PERCOCET®-5 should be cautioned accordingly.

Interaction with other central nervous system depressants Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with PERCOCET®-5 may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, PERCOCET®-5 should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children PERCOCET®-5 should not be administered to children.

PRECAUTIONS Head injury and increased intracranial pressure The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions The administration of PERCOCET®-5 or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients PERCOCET®-5 should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

ADVERSE REACTIONS The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, skin rash and pruritus.

DOSAGE AND ADMINISTRATION Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. PERCOCET®-5 is given orally. The usual adult dose is one tablet every 6 hours as needed for pain.

DRUG INTERACTIONS The CNS depressant effects of PERCOCET®-5 may be additive with that of other CNS depressants. See WARNINGS. 6085 BS

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The Journal of the Maine Medical Association

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Renal Artery Aneurysms*

David M. Sensenig, M.D.

Renal artery aneurysms have been infrequently seen in Bangor in our experience, but the lesions can be of serious import. They may be more common than we realize since Cummings and Associates[1] have found previously unsuspected renal artery aneurysms with the use of selective renal artery angiography in the diagnostic evaluation of patients with suspected renovascular hypertension. We have encountered two patients with this lesion in a two-year period. One was treated electively while the second entered the hospital in shock.

Case Reports

Case 1. A 51-year-old white male was bothered by low back pain. Following ulcer surgery in October of 1975, the patient developed urinary tract infection which responded to treatment but later recurred. An intravenous pyelogram showed a 2 cm. ring-like calcific area in the region of the upper calicyleal area on the right. He had some high blood pressure in the past but had been fairly normal since October 1975.

On physical examination, the blood pressure was 180/110. No abdominal masses were palpable.

Urine analysis was not remarkable, serum creatinine was 0.8 mg. and the BUN was normal. An abdominal aortogram plus a right renal arteriogram showed an aneurysm arising from the superior secondary branch of the right renal artery measuring 3.9 cm. vertically and 2.8 cm. horizontally with a relatively narrow neck measuring 7 mm. The mass possessed some calcification in a curvilinear shape in the periphery but was not uniformly calcified. The aneurysm filled and emptied quickly and had no evidence of clot within it (Fig. 1). The origin of the aneurysm was 1.5 cm. distal to the bifurcation of the main renal artery situated on the more superior branch.

On 3/13/76, excision of the right renal artery aneurysm with a venous patch graft angioplasty was carried out. Care was taken not to obstruct a small arterial branch arising from the area of the aneurysm. Recovery was uneventful.

The patient reentered EMMC on 10/13/76. He had had a dull ache in the right flank during the summer of 1976. An IVP at the referring hospital was reported as showing a delayed nephrogram effect on the right. He entered for an angiogram. His blood pressure was 118/84.

A selective right renal angiogram showed a normal postoperative appearance without stenosis (Fig. 2). An orthopedist found some arthritic change in the spine which possibly explained the back pain. He has had no further difficulty with regard to the kidney.

Fig. 1. Preoperative right renal arteriogram showing aneurysm.

Case 2. An 80-year-old man entered St. Joseph Hospital on 3/27/78 with a history of lightheadedness and syncopal episodes associated with lower abdominal pain of 3 days' duration. The patient had a history of hypertensive cardiovascular disease and had been under treatment for hypertension. The patient fainted in the physician's office and was transferred to the hospital after some resuscitative measures. His hematocrit was 23.

On physical examination, his blood pressure was 60/10, pulse 100, resp. 20. There was a grade 11/VI systolic murmur along the

*From the Surgical Service, Eastern Maine Medical Center and St. Joseph Hospital, Bangor, Maine 04401.

Fig. 2. Postoperative right renal arteriogram.

left sternal border. The abdomen was slightly protuberant in the lower abdomen with tenderness bilaterally more on the right than the left without any obvious pulsating mass.

A KUB film showed no aortic calcification. Emergency operation was undertaken with a diagnosis of ruptured abdominal aneurysm. There was a massive retroperitoneal hematoma extending from the pelvis to the diaphragm. The abdominal aorta was normal in size. There was a ruptured renal artery aneurysm 6 cm. in diameter and a large renal cyst in the upper pole. Because of the distorted anatomy, sclerotic renal vessels, shock, and inability to do any reconstruction during the permitted ischemia time, nephrectomy was necessary. Postoperative problems of retained bronchial secretions and paralytic ileus were overcome so that the patient could be discharged home on 4/15/78. He has done well subsequently.

Discussion

Aneurysms are saccular, fusiform or dissecting and may be intrarenal or extrarenal. According to Smith and Hinman,[2] 17% of renal aneurysms are intrarenal and rupture occurs in 20%. Aneurysms may be traumatic, congenital or a result of periarteritis nodosa. Needle biopsy of the kidney may cause an arteriovenous fistula. Arteriovenous fistula may also result from erosion of an atherosclerotic aneurysm. Dull aching pain is encountered in 50%, hematuria in 10 to 20%, and an abdominal bruit in 20%. Seventy percent are associated with hypertension. Diagnosis may be made from plain abdominal films or by aortography. Associated hypertension may be caused by laminated thrombus narrowing the lumen or obstructing a branch. Segmental arteries may be compressed and there may be alteration of pulse wave due to turbulent flow.

Surgery is indicated for aneurysms 1.5 cm. or larger especially if calcification is incomplete. Operation should be carried out in females who may become pregnant because of danger of rupture. Surgery is indicated for hypertension with renin differentials and for aneurysms with functional or symptomatic impairment.

Surgical treatment calls for excision and closure of the artery. When necessary, the distal branches may be gathered and anastomosed to the main renal artery. Angioplastic or by-pass techniques may be used. Bench surgery[3] with iliac reimplantation may be used if intrahilar or tertiary vessels make this method desirable. At times, nephrectomy, total or partial, may be indicated.

Results are generally excellent with low mortality and good results in controlling hypertension.[4] Dissecting aneurysms of the renal artery are the most damaging to the kidney. The dissection can be corrected surgically.[5]

Summary and Conclusions

The cases described are presented to illustrate an important clinical entity. When there is a curving line of calcification in the renal area further investigation should be carried out to diagnose any renal artery aneurysm so that appropriate operation may be performed in view of the generally good results obtainable.

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Annual Meeting Dates For Your 1979 Calendar . . .

Maine Medical Association, June 16-19

Treadway-Samoset, Rockport, Maine

American Medical Association, July 22-26

Chicago

The Role of Exercise Testing in the Evaluation of Patients With Ischemic Heart Disease*

JOE R. WISE, JR., M.D.

Exercise testing is now frequently used routinely as a part of the evaluation of patients with angina, or chest pain thought to be angina. Exercise stress testing is based on the empirical discovery that exercise in patients with coronary artery disease often produces ST segment depression.[1] Based on this finding, exercise tests like the "two step test" were developed, and follow up observations have confirmed the usefulness of these tests in the detection of ischemic heart disease.[2]

In the past several years, exercise tests using the treadmill or the bicycle ergometer have permitted EKG recordings not only after, but also during the exercise and the amount of exercise could be graded. With the introduction of coronary arteriography, a method of detecting the presence and severity of coronary artery disease became available. Correlation of exercise induced EKG changes with coronary arteriographic findings have allowed better definition of the sensitivity, specificity, and predictive value of the exercise test.[3–8]

The major function of the exercise test is to determine whether or not the coronary circulation can increase oxygen delivery to the myocardium in response to exercise. Since oxygen extraction by the myocardium is nearly complete (70%) at rest, oxygen delivery can be increased significantly only by increases in coronary blood flow. Ordinarily, coronary blood flow increases directly in proportion to increased oxygen demand.[9] In the patient with coronary artery stenosis, however, coronary blood flow may not increase adequately to meet the amount of myocardial oxygen demand and ischemia results, manifest by angina and/or EKG changes. The degree of coronary artery stenosis required to produce myocardial ischemia is disputed, but considered to be between 50% and 75%.[10]

Exercise Test Protocol

Several types of exercise tests have been developed. The single stage test designed by Master uses a predetermined number of trips, based on age, sex and weight over two steps during a one and one-half or three minute period. Although there are limitations to this test, numerous studies have varified its usefulness.[2]

More recently, the Master's Test has been abandoned in favor of the more sensitive and reliable and probably safer multistage or graded submaximal exercise test using the treadmill and continuous EKG monitoring.[11] The protocol developed by Bruce is frequently used. In these tests, the speed and elevation of the treadmill are increased in three minute increments and exercise is continued until 85% of the age predicted maximum heart rate is achieved or until EKG changes or limiting symptoms have developed.[11]

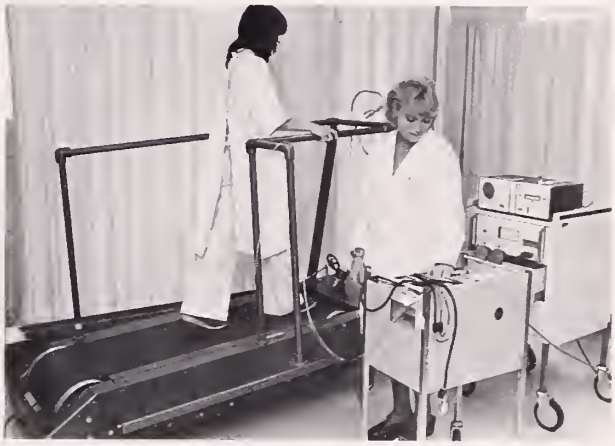

Fig. 1. The speed (0-10 MPH) and elevation (0-20°) of the motorized treadmill can be adjusted according to the requirements of the exercise protocol. The electrocardiogram is continuously monitored on an oscilloscope and resuscitation equipment is immediately available.

A cardiovascular history and examination and 12 lead electrocardiogram are recorded prior to the test. A physician is present during the test and exercise is discontinued with the appearance of signs of exhaustion, limiting chest pain or dyspnea, ischemic EKG changes or rhythm disturbances. Emergency resuscitation equipment including a defibrillator is immediately available (Fig. 1).

As usually performed, the risk of exercise testing is small. In one survey of 170,000 exercise tests, the mortality was 1 per 10,000 tests.[12] Some relative contraindications to exercise testing include recent myocardial infarction, unstable progressive angina, severe hypertensive cardiovascular disease or congestive heart failure, severe aortic or mitral valve disease, uncontrolled cardiac arrhythmia, severe anemia and cor pulmonale.

Correlation with Coronary Arteriography

The results of exercise tests have correlated well

*From the Cardiology Section, Medical Service, Eastern Maine Medical Center, Bangor, Maine 04401.

with the presence of coronary artery disease as demonstrated by a coronary arteriography. In patients with typical angina pectoris and documented coronary artery disease, McHenry found an abnormal or positive exercise test at 85%.[5] For several other studies involving over 1300 patients, the predictive value of the exercise test has been in the range of 87% to 96%.[3]

The sensitivity of the exercise test increases with increasing severity of the coronary artery disease and is to some extent *quantitative*. In Bartel's study, only 40% of the patients with a single vessel disease had a positive exercise test compared with 66% and 76% of patients with two and three vessel disease respectively.[6] When the ST segment change and the exercise *duration* are both considered, the diagnostic value of the exercise test can be further improved. For example, in the study of McNeer, 97% of the patients who had a positive exercise test at Stage I or Stage II (Bruce) had significant coronary artery disease. Sixty percent (60%) of these patients had three vessel disease, and 25% had significant narrowing of the left main coronary artery.[8]

The *degree* of ST segment depression also has predictive value. When no other form of heart disease is present, the deeper the ST depression, the more serious the disease and the worse the prognosis. Thus, if there is greater than 2 mm. ST segment depression, there is a 95% chance that these changes are associated with two or three vessel disease [13 14] and a 70% chance that the patient has three vessel disease or disease of the left main coronary artery.[15] Since the natural history of extensive coronary disease of this type has been worked out,[16] these EKG changes with exercise can be used to estimate the prognosis. Thus, the appearance of 2 mm. ST segment depression with exercise predicts a five year mortality in the range of 40 to 55 percent.[17]

The correlation between stress test results and coronary arteriographic findings has not been as good in asymptomatic patients as in patients with chest pain or evidence of coronary artery disease. The number of false-positives or false-negatives varies considerably with the population study. This is to be expected since the predictive value of any diagnostic test diminishes as the prevalence of the disease declines in a population.[18] In one recent study in which stress test results were compared to coronary arteriographic findings in asymptomatic patients, 48 of 75 patients with abnormal stress tests had coronary artery disease, a predictive value of 65%.[19]

From the data available, comparing coronary arteriography and stress testing, Ellestad has concluded:[4]

1. Subjects with single vessel disease and significant coronary narrowing of 70% of luminal diameter or more have a 40% chance of positive test results.
2. Subjects with two vessel disease have a 65% chance of positive test results.
3. Subjects with three vessel disease have a 78% chance of positive test results.
4. Subjects with left main disease have an 85% chance of positive test results.
5. Subjects with I mm. ST segment depression have a 90% chance of having coronary disease or evidence of significant left ventricular dysfunction.
6. Subjects with 1.5 mm. ST segment depression have a 95 to 96% chance of having coronary artery disease or evidence of significant left ventricular dysfunction.
7. Subjects with 2 mm. or more ST segment depression have a 98% chance of having coronary disease or evidence of significant left ventricular dysfunction.
8. When evaluating subjects with lesser degrees of coronary artery narrowing, the reliability of positive test decreases, but the number of false-negative tests will decrease.

Epidemiologic Studies

Long term observation of patients who have had exercise tests is another method of evaluating the significance of an abnormal response. In a follow up study of 2,003 men, Doyle and Kinch found that, in those whose tests became positive, there was an 85% probability of developing some clinical manifestation of ischemic heart disease within five years.[20] The risk of developing symptomatic coronary artery disease is 14 to 20 times greater for those with positive rather than negative exercise tests.[3] In a study of 2,700 men, Ellestad and Wan found the incidence of new coronary events to be 9.5% per year for those with 1.5 mm. or more ST segment depression, 6% per year for those with 0.5 to 1.5 mm. ST segment depression and 1.7% per year for those with negative exercise tests.[21] McNeer identified a high risk subgroup of patients with an abnormal response in the early stages of the treadmill exercise test who had a subsequent four year mortality of 37%. By way of contrast, those patients who had a negative test, or a test positive in the late stages of exercise, had a four year mortality of 7%.[8]

Based on studies such as these, there seems to be little question that, in asymptomatic subjects, an abnormal treadmill exercise test is predictive of a risk for future coronary events that is 14 to 20 times greater than if the treadmill exercise test is negative.[3]

Indications for Exercise Testing

The indications for exercise testing vary with the nature of the question to be answered and the need to know. In some instances, the results of the exercise test may provide needed reassurance to the patient and physician and at other times stimulate or confirm a major change in treatment.

Evaluation of Patients With Chest Pain

A history of typical angina pectoris usually predicts accurately the presence of ischemic heart disease. As discussed previously, this suspicion can be confirmed, if necessary, with a high degree of reliability. In some patients with chest pain, it is not

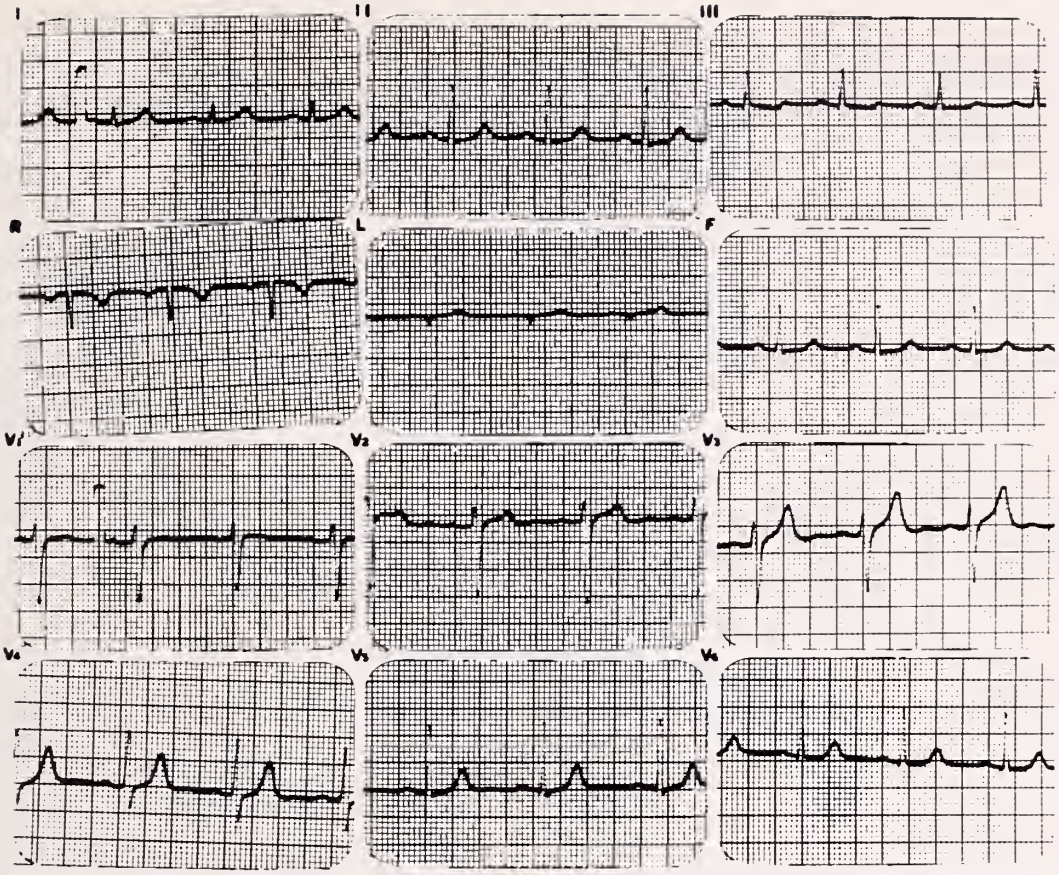

Fig. 2A. The normal resting electrocardiogram of a patient with severe (75%) stenosis of the left main coronary artery.

possible after the usual evaluation to be certain of the origin of the pain and in this group too, the EKG response to exercise can be helpful.

Evaluation of Patients With Coronary Artery Disease

In patients with known coronary artery disease, exercise testing can provide objective evidence of the patient's exercise tolerance prior to the development of symptoms or EKG changes. This information can be used to advise patients about work and exercise limits. Exercise tests are often done for patients following myocardial infarction to reassure them of their exercise capability or to detect residual ischemia which may require treatment. Stress testing is very helpful in evaluating the effectiveness of medical treatment programs for angina or, more recently, the effectiveness of coronary artery bypass surgery.[22]

The exercise test is becoming increasingly useful in the *prognosis* of patients with coronary artery disease. The magnitude of the ST segment depression appears to be an accurate reflection of the extent and severity of coronary artery disease as determined by findings at coronary arteriography which, in turn, are predictors of survival.[14,25] McNeer has stressed the importance of exercise testing in assessing the prognosis of patients with ischemic heart disease.[8] Patients with angina able to tolerate higher levels of exercise on treadmill exercise testing have a favorable prognosis. Patients completing only lower stages have a high prevalence of severe coronary artery disease, a relatively poor immediate prognosis and may be candidates for further study and surgical consideration.

Based on this sort of information, probably all patients with angina should have an exercise test as part of their evaluation. Those with a good exercise tolerance usually have less extensive coronary artery disease, a relatively good prognosis and can be treated symptomatically. Among those patients with a markedly positive exercise test is a group with left main or extensive three vessel disease with a five year mortality in the range of 50%. Some of these patients with extensive coronary artery disease have normal resting electrocardiograms which may be misleading (Fig. 2).

Evaluation of Asymptomatic Patients

Occasionally, physicians, or patients themselves request treadmill exercise tests when there are no symptoms suggestive of ischemic heart disease. Usually these patients are middle aged, sedentary people, who are concerned about their health or wish to engage in an exercise or physical fitness program. It has been estimated that, in this group of patients, in whom one may assume a 10% incidence of a symptomatic coronary artery disease, the predictive value of a negative test provides a 99.4% probability that

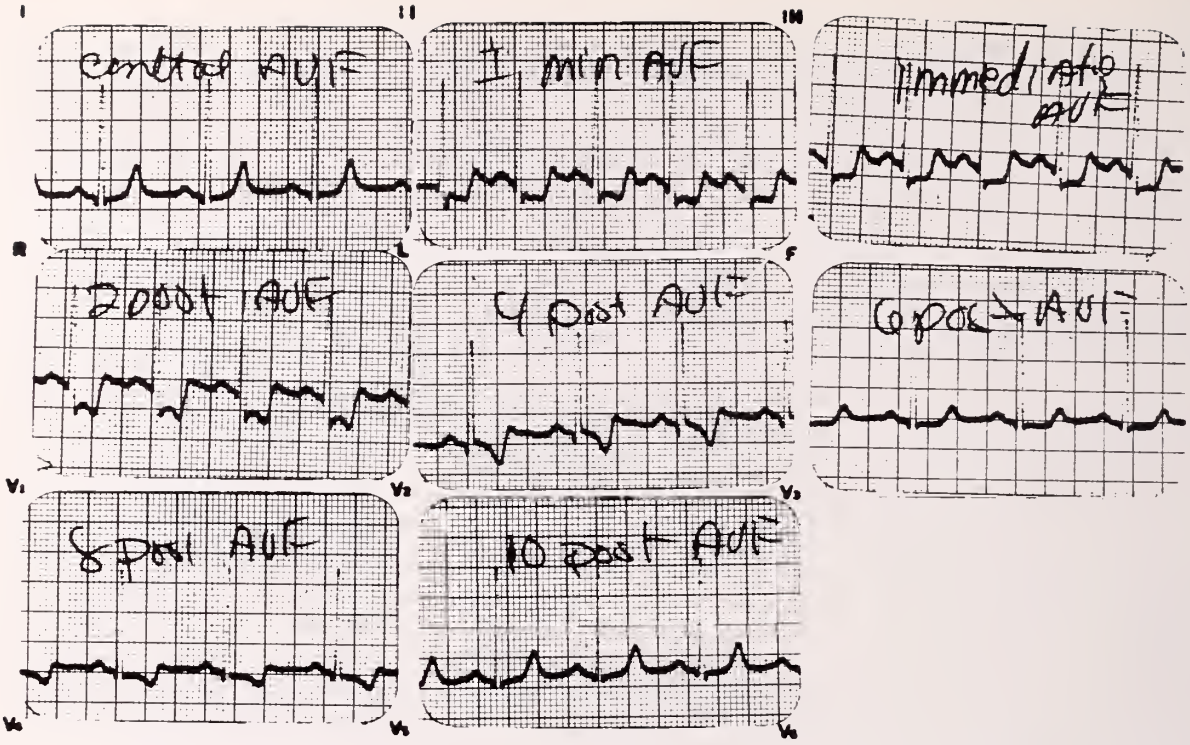

Fig. 2B: Representative recording from the same patient's treadmill exercise test showing marked (3 mm) ST segment depression which occurred after 1 minute of exercise.

the coronary arteriogram will not show evidence of obstructive disease.[23] This is important information since other studies based on serial coronary arteriograms have shown that if coronary artery disease is not present by the fourth of fifth decade, it is not likely to develop subsequently.[24]

Summary

While far from perfect, there is at this time, no noninvasive test superior to the exercise test in predicting the presence or absence of coronary artery disease. In addition, exercise testing is useful in assessing the severity of functional impairment or the effectiveness of a therapeutic program. The demonstration that coronary artery bypass grafting can prolong the life of at least patients with left main coronary artery disease has changed the approach to patients with angina.[26] At present, probably all patients with angina should have an exercise test as part of their evaluation. Those with markedly positive tests, as indicated by prominent ST segment depression or pain very early in the test, have an increased risk of left main coronary artery disease and should be considered for coronary arteriography.

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Wolff-Parkinson-White Syndrome

Evaluation of a Potentially Life Threatening Situation*

ROBERT M. HOFFMANN, M.D.

CASE SUMMARY

Patient M.N. is a 25-year-old male with known Wolff-Parkinson-White (WPW) syndrome since 1972. All electrocardiograms have shown type B WPW (Fig. 1). Because of a history of intermittent tachy-palpitations felt, but never documented, to be supraventricular tachycardia, he was given digoxin in 1972. He continued to be bothered with rare episodes of tachy-palpitations approximately 3 to 4 times per year which produced symptoms of mild light-headedness and could apparently be terminated after a brief period with a modified Valsalva maneuver. Two weeks prior to admission after scuba diving, he experienced a chill rapidly followed by a more severe and protracted bout of tachy-palpitations with near syncope. This bout could not be terminated by the usual maneuvers. He sought medical assistance and an EKG was done (Fig. 2). In route to a local hospital, he vomited and converted to sinus rhythm.

Because the electrocardiogram was felt to represent atrial fibrillation with atrioventricular conduction through an atrioventricular bypass tract with a resultant rapid ventricular response producing a potentially life threatening situation (Shortest RR-160 milliseconds and average ventricular response 310), he was admitted to the Eastern Maine Medical Center for further evaluation. Digoxin had been discontinued one week prior to admission. The past medical history was otherwise negative. The physical examination was unremarkable.

On the day following admission, the patient was brought to the catheterization laboratory in a fasting state. He had received 300 mg of disopyramide phosphate (Norpace®) one hour prior to the initiation of the study. An intravenous line had previously been inserted in a peripheral vein. Through the right femoral vein two USCI #5 french bipolar pacing catheters were inserted. The first was positioned in the right ventricle in the region of the Bundle of His and used for recording purposes. The second was positioned in the lateral right atrium for atrial pacing. Using a standard Model #5880 Medtronic® temporary pacer, the right atrium was paced intermittently at approximately twice threshold until atrial fibrillation was induced. The recordings were taken from the pacing catheter and two standard electrocardiographic leads on a Electronics for Medicine recorder (Fig. 3). The patient was moderately light-headed during this episode (Shortest RR 210 milliseconds. Average ventricular response 216) which terminated spontaneously after approximately 15 minutes. Lidocaine 100 mg intravenous bolus was given with no significant change in the ventricular response. The ventricular catheter was removed and the atrial catheter was left in the inferior vena cava. The patient returned to the ward. Approximately 4½ hours after the disopyramide phosphate dose when a therapeutic serum drug level was probable, he returned again to the catheterization laboratory. The pacing catheter was repositioned in the right atrium and atrial fibrillation was again induced (Fig. 4). It spontaneously terminated in less than 5 minutes (Shortest RR 300 milliseconds. Average ventricular response 186).

It was felt that digoxin had dangerously shortened the effective refractory period of the bypass tract and therefore was contraindicated. The effective refractory period remained short off medication and because disopyramide phosphate lengthened this and slowed the average ventricular response, the patient was discharged taking disopyramide phosphate 150 mg 4 times a day.

DISCUSSION

The WPW syndrome was first recognized as a clinical entity in 1930.[1] The syndrome was characterized by an anatomical connection separate from the AV node between the atria and ventricles capable of conducting electrical impulses in an antegrade or retrograde direction. Forty (40%) to eighty (80%) percent of these patients are troubled by tachycardias of varying duration, rate and symptomatology.[2] Seventy-five (75%) to eighty (80%) percent of these tachycardias are reciprocating (circus rhythm) tachycardias also called PAT utilizing the AV node in an antegrade fashion and the bypass tract in the retrograde fashion or vice versa.[3] The remainder of the tachycardias are atrial fibrillation or flutter.[3] The degree of ventricular excitation through the bypass tract or AV node during atrial fibrillation or flutter depends in part upon the refractory periods of each pathway and the degree of concealed conduction in each.[4] Atrial fibrillation is more common in patients with WPW syndrome as compared to the general population.[5] In addition, atrial fibrillation is more common in patients with type A than type B.[4]

Sudden death has been described in the WPW syndrome and in some cases has been clearly related to atrial fibrillation in patients with short effective refractory periods in the bypass tract.[4,6] The short effective refractory period permits rapid stimulation through the bypass tract of the ventricles at times in excess of 300 beats per minute potentially exciting the ventricular during the vulnerable period leading to ventricle fibrillation.[6]

It would obviously be of importance to identify the patients with WPW syndrome with short effective refractory periods at risk of developing atrial fibrillation with rapid ventricular responses. Unfortunately, these patients may have no prior history of tachy-palpitations.[6] In addition, patients with a history of documented reciprocating tachycardias may spontaneously convert to or develop atrial fibrillation.[7] Using certain sophisticated equipment (programmed electrical stimulators) one can with pacing catheters insert extra stimuli progressively earlier in the cardiac cycle and determine the effective refractory period of the bypass tract. This correlates well with the shortest RR interval during the atrial fibrillation.[8] There are limitations to this technique due to the refractory periods of the atria and ventricles.[9] Another useful method is the elective induction of atrial fibrillation[9] which was done in the case presented. With either method, having determined the effective refractory period the bypass tract, one can then administer various cardiac drugs to assess their effect on the refractory period.

Digoxin has been shown to have a variable effect on the bypass tract effective refractory period but certainly in some instance will shorten it producing a

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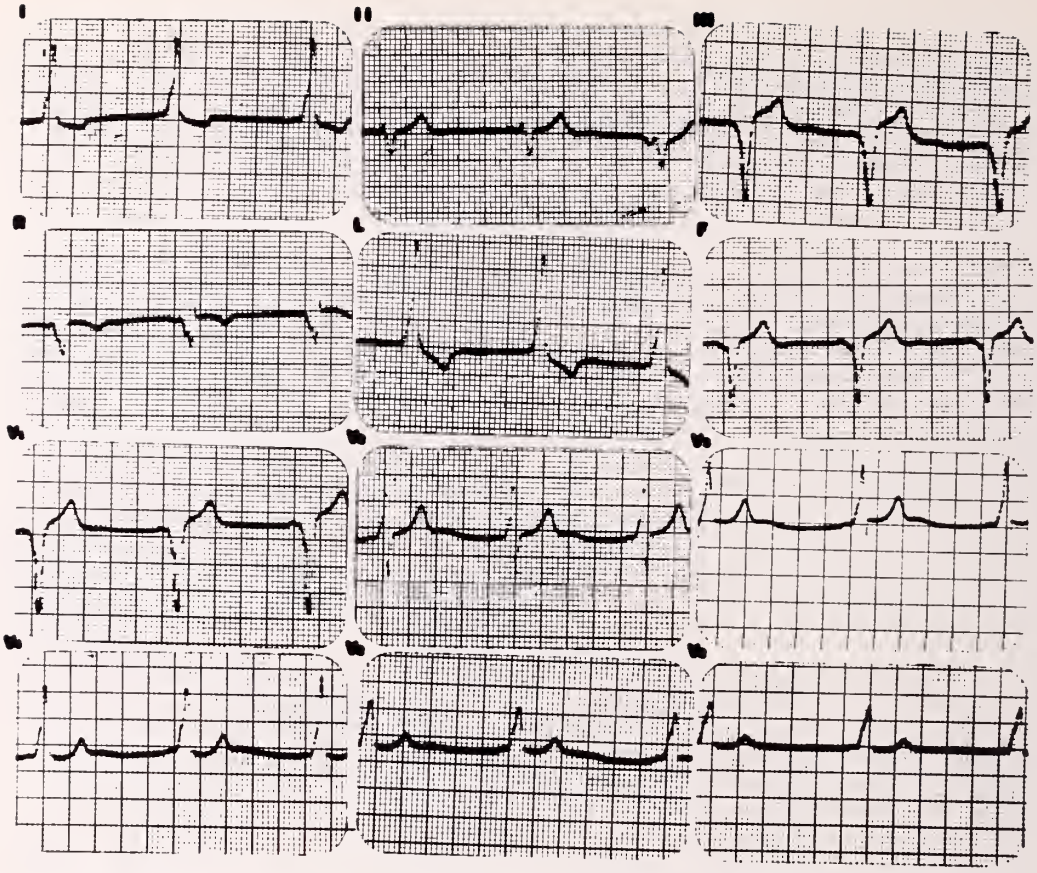

Fig. 1. Twelve lead electrocardiogram on patient M.N., showing type B Wolff-Parkinson-White syndrome.

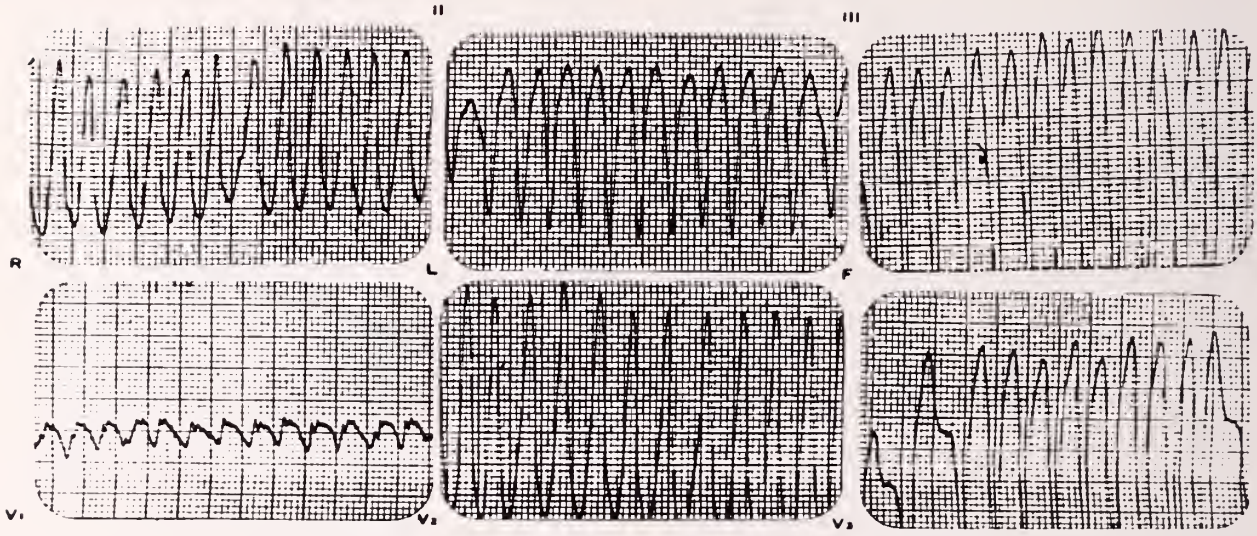

Fig. 2. Bout of atrial fibrillation after scuba diving while on digoxin.

life threatening situation during atrial fibrillation.[9] One, therefore, tends to avoid the use of this drug, although frequently useful in the WPW syndrome, unless its effects on the bypass tract has been studied.

Most cases of ventricular fibrillation have been noted with the shortest RR interval during atrial fibrillation less than 220 milliseconds, but one would be concerned if the shortest RR interval during atrial fibrillation was then 300 milliseconds.[9] Obviously not all patients with WPW syndrome need determination of their effective refractory period. Certainly those patients with documented ventricular fibrillation or rapid atrial fibrillation requires study. In addition, those with a history of syncope or significant symptoms during periods of tachy-palpitations probably would require study. Twenty-four hour Holter monitoring would also be valuable in evaluation of these patients. Patients with documented reciprocating tachycardia controlled on medications or asymptomatic patients probably do not require study. Pa-

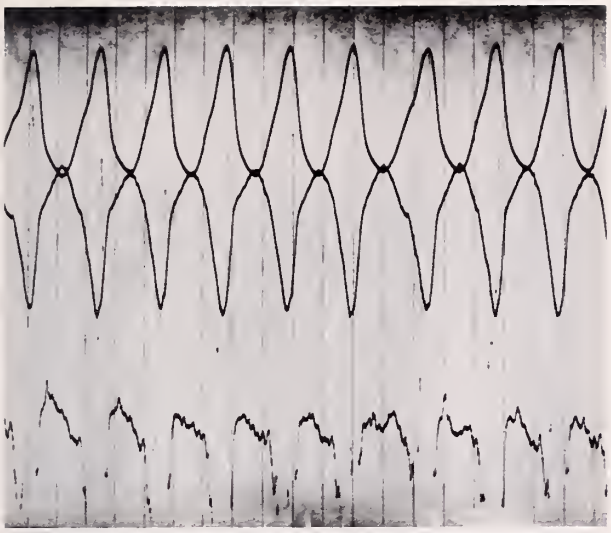

Fig. 3. Induced atrial fibrillation off medication. Standard electrocardiographic limb leads I, III, and intracardiac recording. Paper speed: 100 mm/per second.

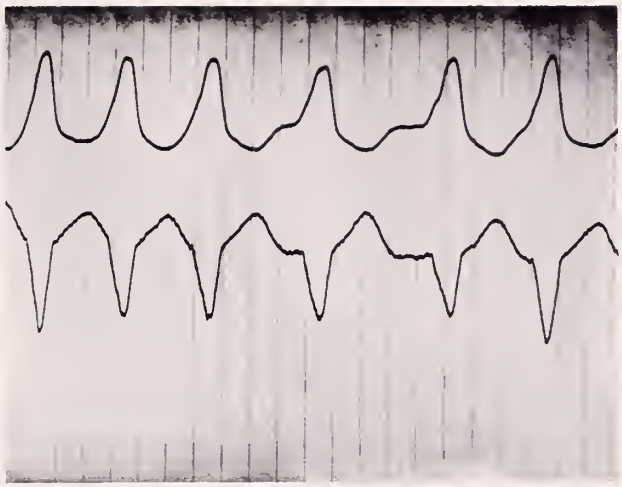

Fig. 4. Induced atrial fibrillation while on disopyramide phosphate. Electrocardiographic leads I and III. Paper speed 100 mm/per second.

tients with refractory reciprocating tachycardias require more detailed electrophysiological studies which would probably include effective refractory period determination. Whether patients with WPW syndrome with certain positions of responsibility such has pilots or bus drivers require study is open to debate at this time.

As noted the extra stimulus technique utilizes expensive and sophisticated equipment for a procedure not likely to be often required. On the other hand, elective induction of atrial fibrillation requires no special equipment than what is generally available at most regional medical centers, i.e., electrocardiogram machine, temporary pacemaker, fluoroscopy and a defibrillator. This procedure can be performed at acceptably low risk.[9] The patient must be informed that defibrillation or cardioversion may be necessary.

Having identified a short effective refractory period and, therefore, a patient at risk of sudden death, various antiarrhymic agents can be given and the effective refractory period rechecked. Drugs available in this country known to lengthen the effective refractory period of the bypass tract include: quinidine,[10] procainamide,[10] and lidocaine.[11] Unfortunately the response can be variable and needs evaluation in the individual patients. Drugs currently not available in this country, also known to be effective, include amiodarone[12] and ajmaline.[3] If the available drugs prove ineffective or only partially effective, then consideration must be given to surgical interruption of the bypass tract[5] which requires detailed electrophysiological study.

In the case presented it certainly appeared that digoxin dangerously shortened the effective refractory period. Disopyramide phosphate was tried since its effects are similar to quinidine with less frequent side effects.[13] Disopyramide phosphate appeared to satisfactorily lengthen the effective refractory period in this patient. In addition, disopyramide phosphate has been shown to decrease the frequency of atrial fibrillation which also would be beneficial in this type of patient.[14]

Summary

A case of WPW syndrome with atrial fibrillation with a dangerously fast ventricular response was presented with evidence that digoxin inpart contributed to this by shortening the effective refractory period of the bypass tract. In addition it was shown that disopyramide phosphate (Norpace) lengthened the refractory period and slowed the ventricular response. The implications of atrial fibrillation in the WPW syndrome and its evaluation using elective induction of atrial fibrillation were discussed. The procedure is simple, effective, and can be performed at regional medical centers without additional expensive and infrequently utilized equipment.

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Primary Foreign Body Peritonitis*

GEOFFREY M. GRATWICK, M.D.** AND KANWALCHARAN SINGH SAHNI, M.D.

ABSTRACT

At diagnostic laparotomy, a forty-five-year old man with transudative ascites showed miliary nodules studding his peritoneum. On histologic section, these were found to contain vegetable matter, characterized by double cell walls, which was surrounded by giant cells and fibrous tissue. The patient is currently alive and well.

Primary peritonitis associated with miliary nodules in the peritoneal cavity is frequently due to carcinomatosis in the United States[1], but may be a manifestation of tuberculosis[2] or helminth ova in other parts of the world.[3] We have recently cared for a man with primary peritonitis in whom we found miliary nodules containing vegetable matter spread throughout the peritoneum.

CASE REPORT

A forty-five-year old blind mosque attendant was admitted to the Medical Service of Saadi Hospital, Pahlavi University, complaining of increasing abdominal pain and swelling of one month's duration. He had been in general excellent health throughout his life except for trachoma in childhood which had left him with bilateral corneal scarring and total blindness. He did not smoke or drink and took neither Western nor traditional medicines.

A year prior to admission the patient reported a febrile illness with weakness, anorexia, and profuse sweating. Approximately a week later he experienced the sudden onset of diffuse severe abdominal pain, worse than he had ever known. No specific therapy was administered, and the pain slowly remitted over the next two weeks. His fever gradually abated over six weeks leaving him weakened and listless. At no time did he have right upper quadrant tenderness, glandular swelling, constipation, diarrhea or persisting night sweats. He was not told of a skin rash or ankle swelling. There was no known contact with hepatitis and no one else in his village had a similar illness. The patient recovered slowly but never completely regained his former strength; a month before admission he noticed the onset of abdominal swelling.

On admission, the patient was a chronically ill-appearing man who was alert and well-oriented. Ascites with dilated abdominal veins, a 1 x 1 centimeter right axillary lymph node, and corneal scarring were present. He was afebrile and had normal chest, neurological, skin, and rectal examinations. There were no abdominal scars or wounds.

White blood count was 11,000 (polymorphonuclear leucocytes [PMN] 68, band forms 4, lymphocytes 25, monocytes 1, and basophils 1); hemoglobin, 11.0 gm%, prothrombin time, 15 seconds (control was 13 seconds), SGOT, 19 Karmen units/ml, albumin/globulin, 2.0/4.5 gm%, alkaline phosphatase, 6.2 Bodansky units, negative lupus erythematosus cell test, negative Widal test, negative intermediate strength PPD, and negative stool guaiac; stool examinations failed to detect parasites or helminth ova and no acid-fast bacteria were seen in 3 sputum specimens. He had a normal serum creatinine, amylase and urinalysis. An abdominal paracentesis revealed cloudy fluid with a specific gravity of 1.008, protein of 1.8 gm%, cholesterol of 16 mgm%, and white blood cell count/mm³ of 1103 (PMN 55% and lymphocytes 45%). Cytological examination did not reveal malignant cells and aerobic and anaerobic cultures were sterile. Cultures for M. tuberculosis were also negative. A chest x-ray showed no evidence of apical or hilar abnormalities and cholecystogram and x-ray contrast studies of the esophagus, stomach and small and large intestines were normal. Fiberoptic endoscopy was performed and revealed a normal stomach, antrum and pylorus without evidence of scarring. A biopsy of the enlarged right axillary node showed normal lymph tissue.

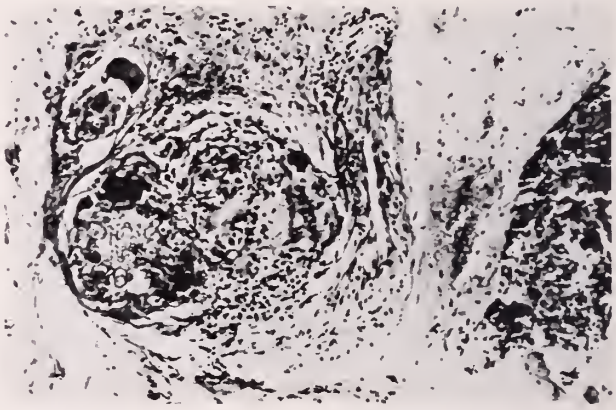

Fig. 1. Peritoneal granuloma with giant cells and fibrous tissue.

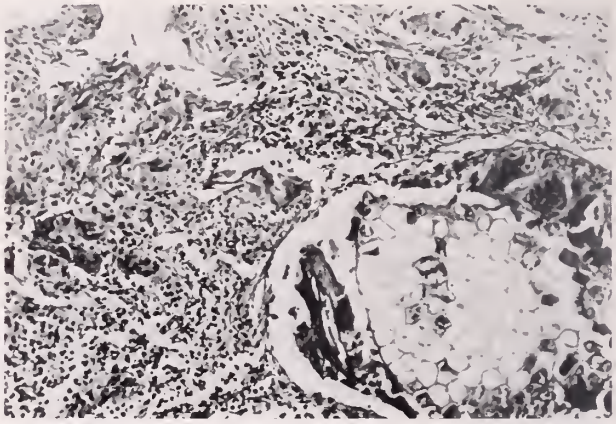

Fig. 2. Peritoneal granuloma surrounding double walled plant material.

To rule out malignancy or an atypical presentation of tuberculosis, the patient underwent an exploratory laparotomy. His bowel was fused into a dense mat with widespread adhesions connecting the bowel, omentum, liver, and spleen, and there were multiple hard miliary nodules on the parietal and visceral peritoneum grossly resembling those seen in tuberculosis peritonitis. Several of the nodules and the liver were biopsied. Post-operatively, oral anti-tuberculous treatment was begun.

The liver was histologically normal. Multiple sections of several nodules revealed granulomas with giant cells, lymphocytes and fibrous tissue surrounding double walled vegetable fragments. Cultures of those nodules were negative for AFB (Figs. 1 and 2). Anti-tuberculous treatment was stopped and the patient discharged on diuretic treatment. Six months later he sent a letter from his village offering us a gift of eggs and chickens and stating that he felt well.

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Comment

Initially the diagnosis in this patient with ascites was felt to be tuberculous peritonitis, cirrhosis or malignancy. The negative intermediate strength PPD and the transudative character of the ascites made tuberculosis unlikely.[2] The low albumin, elevated alkaline phosphatase, and clinical status were compatible with cirrhosis but the cell count in the ascitic fluid was high. Parisitic disease could not be demonstrated on multiple stool examinations.

The findings at laparotomy of vegetable matter in peritoneal nodules make it reasonable to assume that the patient had a self-limiting perforation at some time in the past. Intraperitoneal vegetable matter with surrounding granulomas has been reported infrequently.[3] Askenazy[4] described a forty-eight-year old stable man who was kicked in the abdomen by a horse and began to cough up foul sputum six weeks later; after three months he died with unrelenting fevers. Autopsy revealed perforation of the caecum, several loculated intraperitoneal abscesses, and empyema of the right chest. There were small nodules scattered throughout the peritoneum and on histological section, giant cell granulomas with a great deal of fibrous tissue were seen surrounding vegetable particles characterized by double walls.

It is uncommon for a person to leak vegetable matter into the peritoneal cavity and survive. It is unlikely that this patient had unremembered trauma of such severity as to cause perforation. It is possible a perforation had complicated a peptic ulcer, which had since healed. Typhoid fever may cause intestinal perforation but usually has a fatal outcome; Osler reported that his patients with typhoid and intestinal perforation "almost invariably" died[5] while Keen reported that 96% of his typhoid patients with perforation died.[6] The diagnosis of typhoid is uncommon but not impossible in the presence of a negative Widal test.[7] As this patient is doing well at last report, it is unlikely that we shall have further opportunity to investigate his problem.

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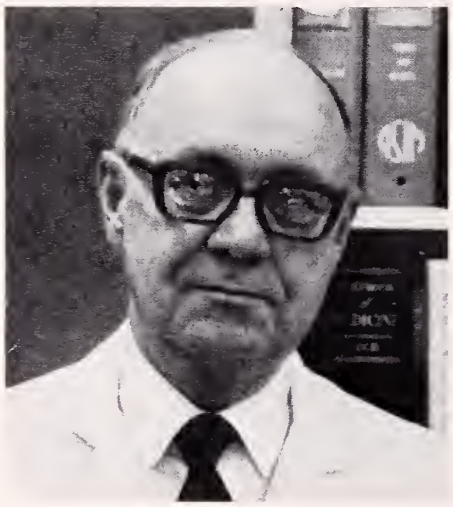
"THE PHYSICIAN IS A DECISION MAKER, AND ALMOST EVERY DECISION HE MAKES COSTS OR SAVES MONEY."

—Dr. William Felts, Past President, American Society of Internal Medicine



More and more physicians today are beginning to realize the extent of the economic influence they have, and are finding ways of holding costs down.

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**PATIENT CARE Magazine—Outlook 1977, "Face-Off: Cost Containment vs. Chaos," January 1, 1977*

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Laboratory Study of Commonly Used Microvascular Clips*

Mary J. C. Blaschke, B. S.,** Carroll P. Osgood, M.D.† and James S. Huston, Ph.D.**

Abstract

Microvascular clips are essential for conducting microsurgical procedures in digital replacement and other types of microvascular surgery. However, the vast majority of these clips have never been objectively compared to evaluate the extent of vascular damage created by their application. We have examined the degree of intimal damage resulting from use of most standard microclips with scanning electron microscopy (SEM). Severe damage is produced by nearly all clips commonly used, and only one design was found to be completely atraumatic by analysis with SEM.

Introduction

The clips initially used for temporary occlusion in microsurgery were generally small neurosurgical aneurysm clips. These were intended for the permanent occlusion of arterial aneurysms, and it is now widely appreciated that these clips cause significant endothelial damage when used even briefly on small vessels.[1]

Over the past five years, surgical supply houses have manufactured a variety of new clips, especially designed for temporary small vessel occlusion in the expanding field of clinical microsurgery.[2,3] It is difficult for the surgeon to select the least traumatic clips available commercially, as most are attractively cataloged, and expensive. We have studied the current generation of these microclips from two standpoints: first, the actual mechanical force developed by each clip was measured, and compared to the theoretical pressure calculated as needed to occlude small arteries.[1] Second these same clips were used on rat carotid arteries which were then viewed on a scanning electron microscope (SEM). The clip models were then compared for endothelial trauma discernible on SEM.

The Kutz-Kleinert® clips were associated with minimal endothelial SEM changes and developed less closing pressure than any other clip examined.

Materials and Methods

This study utilized adult Sprague-Dawley rats of both sexes weighing 300-500 grams. Each rat was anesthetized with intraperitoneal pentabarbital, 35 mg/kg. Using microsurgical techniques, both carotid arteries were exposed, and a microvascular clip was applied to each artery. The clips were left in place for 30 minutes, the usual length of time for a clinical anastomosis. After the clips were removed, each carotid segment was carefully excised and opened longitudinally with microscissors. The artery was immediately rinsed with normal saline and placed in 6% glutaraldehyde for 24 hours. Specimens were then dehydrated by serial passage through 50% to 100% ethanol. Next the specimens were dried with a standard critical point drying apparatus, and mounted on small aluminum studs which had been coated with a carbon colloid. Specimens were put into a vacuum chamber where a 250 Å layer of gold-palladium was applied.

Each specimen was then examined at magnifications of 20-20,000X using the AMR 1000A Scanning Electron Microscope. All of the photographs were taken with a Polaroid camera through the scanning electron microscope. Each clip was tested on four arteries and only the reproducible damage was noted.

In addition to the SEM evaluation, the force required to open each clip was measured. Progressively increasing weight was suspended to the lower jaw of each clip when it had been clamped in place. The distal ends of the jaws were viewed with the operating microscope and total mass noted when they were parted 1.0 mm. Results were highly reproducible for single clips with forces greater than 60 grams. Double clips on adjustable frames, did not have equal closing forces, and clips with forces believed to be less than 15 grams could not be measured accurately in this fashion. For comparison, the minimum force required to occlude small arteries was calculated using the formula given by Dujovny, et al[1]: Force is equal to the product of the blood pressure expressed in grams/mm^2 and the area on which that force is exerted. The mean blood pressure for man is only slightly higher than the mean pressure in rats, which typically is 100 mm Hg, or 1.36 gm/cm.^{2} To occlude a rat artery which is 1 mm in diameter, a microclip that is 1.5 mm wide must exert at least 3.2 grams of force. Even if the mean blood pressure is raised to 210 mm Hg, the minimum occlusion force is only 6.7 grams.

Results

Normal rat carotids (1.0 to 1.5 mm diameter) to which no clips had been applied, were compared with the experimental arteries. The normal arterial endothelium had a smooth undulating pattern of ridges and folds. These folds were about 10μ in width (Fig. 1).

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Fig. 1. Control artery showing normal endothelial folds. (180X)

Fig. 2. Scanning electron micrograph of artery to which Mayfield clip was applied. (500X)

Fig. 3. Scanning electron micrograph of artery to which Holco clip was applied. (480X)

Fig. 4. Scanning electron micrograph of artery to which Acland clip was applied. (720X)

The endothelial ridges and folds were completely obliterated in all specimens to which a miniature Mayfield® clip was applied. In addition, the edges of this clip produced severe lacerations where fibrin, platelets, and red blood cells were heavily deposited (Fig. 2). Temporary occlusion by the Holco® clip produced a similar degree of damage (Fig. 3); although this toothed clip did not flatten the endothelial folds, as did the Mayfield clip, sharply defined transverse lacerations were observed on these specimens outlining the clip's edges.

Arteries occluded by double Acland® clips at high magnification showed, at high magnification, flattening of endothelial folds, but these folds were not disrupted (Fig. 4). Some of these double Acland clips are mounted on small wire frames, believed to be the cause of the characteristic grooves seen on these specimens (Fig. 5). Because small double Acland clips are somewhat more cumbersome to apply than are single clips, additional manipulation of these delicate vessels is required.

Larger Kapp® clips (serrated) developed the greatest closing force; after alteration of the spring the clip exerted less than 25% of its original force.

Fig. 5. Scanning electron micrograph of artery to which Acland with frame was applied. (180X)

Fig. 6. Scanning electron micrograph of artery to which KAPP clip was applied. (500X)

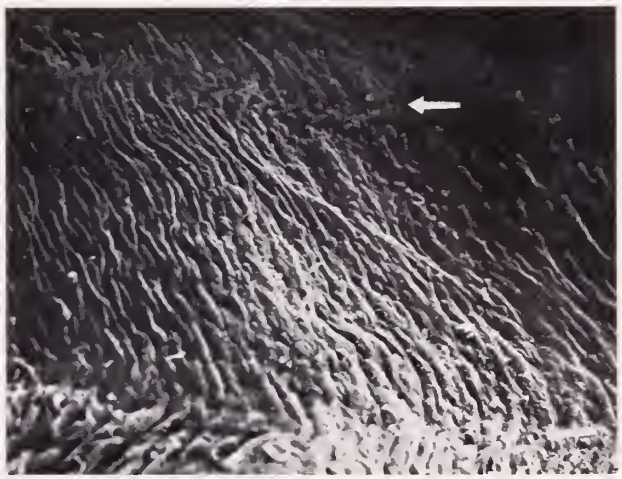

Fig. 7. Scanning electron micrograph of artery to which LINK clip was applied. (210X) Two horizontal compressions are marked by arrows.

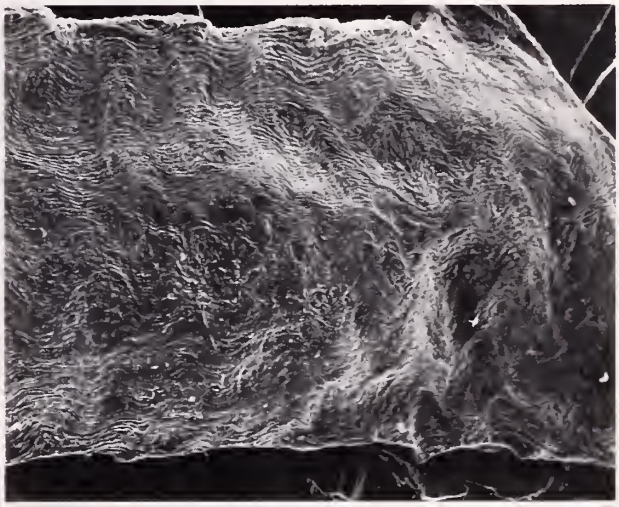

Fig. 8. A curved KK clip, manufactured by the Weck Co. (#065145) was applied to this specimen. No endothelial damage was produced. (Magnification 48X)

This "half-sprung" clip still produced endothelial damage (Fig. 6), and in the most seriously disrupted areas early thrombus formation could be seen.

Arteries that had been occluded by a large double clip (LINK® Company), revealed four parallel troughs of compressed endothelial ridges, but endothelial continuity was preserved (Fig. 7).

The least traumatic clips were clearly the Kutz-Kleinert clips, as temporary occlusion with KK clips produced no discernible endothelial disruption (Fig. 8).

Discussion

Most of the clips we examined produced intimal damage, and most damaged specimens showed two parallel lesions, one slightly more severe than the other. Since the distance between them was comparable to clip width, it appears the clip edges cause this damage.

A wider metal clip with enough curve to eliminate the cutting force from the clip's edges seems desirable. It also appears that longer clips would have more versatile use, since the closing force of a clip decreases exponentially as the distance from the fulcrum point increases.[1] Another aspect to be considered in clip design is the ease of application. Generally the placement of two single clips requires less twisting and other potentially harmful manipulation than that which is required for the placement of double clips with frames. The impartial laboratory scrutiny of new surgical technology remains important.

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Maine Medical Association

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Continued on Page 346

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Necrology

Chester F. Hogan, M.D.
1907-1978

Dr. Chester F. Hogan, 71, of Houlton, Maine, died on August 25 in a Hartford, Connecticut hospital.

He was born in Houlton on March 26, 1907, the son of Frederick A. and Jennie E. Hogan.

Dr. Hogan was graduated from Bowdoin College and received his medical degree from Boston University School of Medicine in 1930. His postgraduate courses included the Bridgeport Hospital and Manchester Memorial Hospital.

He practiced in Mars Hill and Portland, and located in Houlton where he was a staff member of the Houlton Regional Hospital. During World War II, he served in the U.S. Navy Medical Corps as a Commander.

Dr. Hogan was a senior member of the Aroostook County Medical Society and the Maine Medical Association, and was certified by the American Board of Otolaryngology.

Surviving are his widow, Ann E. Hogan of Houlton; one son, Joseph Hogan of Houlton; five daughters, Mrs. Patricia Pingree of Boston, Massachusetts, Miss Mary Hogan of Denver, Colorado, Mrs. Jane Brown, Mrs. Margaret Hagan and Miss Kathleen Hogan, all of Houlton; and one granddaughter.

County Society Notes

York

The May meeting of the York County Medical Society was held on May 10, 1978 at the Webber Hospital in Biddeford.

The program had its usual format with a social hour from 6:30 p.m. to 7:30 p.m. Following a delicious dinner, we had an excellent and well-versed speaker who gave an outstanding talk on "Review of Current Trends in Legislation Affecting Health Care." He was Grant Heggie, who is a senior Vice President of the Maine Hospital Association. He has a wealth of experience in health planning and hospital administration. His speech was enthusiastically received by all those present and it evoked considerable discussion.

The business meeting ensued after this presentation. The meeting was called to order by Dr. Bacon, Secretary, in the absence of Dr. Hazzard, President of the York County Medical Society. The reading of the minutes of the March meeting was dispensed with. There was no old business or new business. There were, however, several announcements made and these included:

1. The Annual Meeting of the Maine Medical Association to be held at Rockport, Maine from June 10 to June 13, 1978 at the Treadway-Samoset.

2. The next meeting of the York County Medical Society is to be held at the York Hospital, York, Maine. The date has been changed to Wednesday, October 18, 1978. The committee appointed to be in charge of this meeting includes: Dr. Kenneth Leigh as Chairman, assisted by Dr. John Leonard and Dr. Alvin Hoffman.

Other items of importance included a report of the Interim Meeting of the House of Delegates of the Maine Medical Association by Dr. Carl Richards. This was on Saturday, March 18, 1978 at the Eastern Maine Medical Center in Bangor. He presented a resolution, presented to the York County Medical Society in March by Dr. Irvin Dorfman. This resolution is as follows:

Whereas: Reimbursement for medical services has been assumed largely by third-party agencies, and

Whereas: Grievances concerning fee levels, turnaround time of claims, eligibility, etc., are becoming increasingly difficult to gain a fair hearing.

BE IT RESOLVED: That the Maine Medical Association establish an office to receive, document and arbitrate complaints of physicians regarding their relations with third-party payers, there being currently no other resources available except the courts of law.

Estimated Cost: *$25,000 - $30,000*

Source of Funds: *General Funds*

It was mentioned that Dr. Dorfman will be at the Annual Meeting of the House of Delegates in June at the Treadway-Samoset to discuss and defend this resolution. It should be mentioned here that he has submitted the necessary criteria and details that will make it conform to all requirements needed to be presented at the Annual Meeting. I must say that some very strong words were used.

Dr. Richards also spoke about the budget for the coming year and also mentioned that there is one nomination for President-Elect, Dr. Brinton Darlington. There is no nominee needed from our district this year for the Executive Committee. In addition, Dr. Richards presented resolutions from various County Societies and the Executive Committee, also to be presented at the Annual Meeting.

Dr. Richards also reported on material presented by Dr. Douglas Hill, President of the Maine Medical Association. It included the "Certificate of Need" and the 10 percent Medicaid cut. This also included material about the Maine Medical Association Committee on Health Care Financing which was to meet on March 22, 1978 to discuss the revision of the Medicaid fee schedule and urged the delegates that specialty groups submit their suggested fees if they haven't already done so.

There were twenty-one physicians and three guests present.

The meeting was adjourned approximately at 9:45 p.m.

Melvin Bacon, M.D., *Secretary*

Washington

The regular meeting of the Washington County Medical Society was held on May 11, 1978, at the Lincoln House Country Inn, Dennysville, Maine, with nine (9) members and guests present.

Dr. James C. Bates, President of the Washington County Medical Society, introduced Dr. Jeremy R. Morton of Portland, Maine, who spoke on Maine Medical Mutual Insurance Company. Dr. Morton gave a brief history of the development of the malpractice insurance organizations. He mentioned the JUA, Joint Underwriters Association, which covers the doctors unable to find insurance with other companies. The doctors from the Maine Medical Association were desirous of setting up their own insurance company. Committees were established and the Maine Medical Insurance Co. gradually evolved from this. This has been over approximately a three-year period. Fortunately, during that time, they have had the opportunity to watch companies developing in other states and have benefited from their experience. They first sent out notices to all physicians, and approximately 75% responded, saying they would be interested in joining this type of insurance company. This company has no connection with the Maine Medical Association. It has to accumulate enough capital interest to be ten (10) times occurred limits. It is set up with the guidance of Johnson & Higgins, consulting firm and also use of a legal firm, plus one of the Portland based banks. Dr. Morton stated that the insurance plan would be a "claims made" type and hopefully would cover physicians when they retire. Initial limits would be $100,000.00 to $300,000.00. It would also cover office personnel. They had hoped to start issuing policies by July 1, 1978. At present, the final approval is awaiting the Maine Insurance Commissioner, who has had the papers for approximately three (3)

months. They are awaiting action. They have tried to make the Board of Directors representative of the whole State, as well as various fields of practice, with all men in the program active in practice. The insurance prospectus will be sent to every physician, as soon as they have a final approval. There was some discussion with many questions asking Dr. Morton about the insurance. It was favorably received.

The minutes of the last meeting of the WCMS were read and approved.

Discussion of the Washington County Health Plan. The members generally opposed a new WCHP Grant Proposal and will so notify Marshall Frankel of the Regional Board in Boston, Mass.

Dr. Bates stated that the Liaison Committee of the WCMS, consisting of Drs. Hazen Mitchell, Carl Aselton, Jr. and G. Bernard Shaw met with the WCHP to discuss this grant and other matters.

Also discussion of the Down East Health Service, with a thought that we should take more interest in their activities, some of which are counter to the original plans.

The meeting adjourned at 10:00 p.m.

KARL V. LARSON, M.D., *Secretary*

Hancock

The Hancock County Medical Society meeting was held on April 12, 1978 at the Hilltop House in Ellsworth.

Members present were Drs. Tyler, Haynes, Gurnee, McIntyre and Bromley. Others present were the speaker, Mrs. Joan Larsen of the Hancock County Planning Commission, and the wives of the members.

The new officers were introduced:

President, Dr. John R. Tyler, Blue Hill

Vice-President, Dr. Ormand L. Haynes, Jr., Bar Harbor

Secretary-Treasurer, Dr. Quinby D. Gurnee, Winter Harbor

Delegate to the M.M.A. House of Delegates: Dr. Chester W. Howe, Blue Hill. Alternate: Dr. George G. Fuller, Sullivan

Dr. Tyler wishes to: 1) formulate meeting times perhaps by polling members; 2) inform new M.D.'s in area; 3) adopt mechanism whereby no dues obligations are there for first year; and 4) send letter to membership that we did elect officers.

Dr. Haynes feels meeting talks should be relevant to all M.D.'s rather than educational—better to be political (insurance, etc.) Dr. McIntyre agrees. Dr. Bromley thinks since our money goes to the State Society, the State Society should provide us with programs.

Dr. Gurnee asks that past officers clue in new officers. Discussing Dr. Tyler's recommendations, it was felt the State Society can inform us when new M.D.'s come into area. We can aim for the first Wednesday in May for our next meeting.

The Hancock County Planning Commission is a clearing house and must give approval to all federal grants. Mrs. Joan Larsen wishes the county society to give input. Of the first $120,000, $80,000 went for salaries. Dr. McIntyre will be appointed by Dr. Tyler to be the representative. Dr. Tyler wants Dr. McIntyre to contact Mrs. Larsen with the idea of having her speak to the County Medical Society meeting. Dr. McIntyre explained the Hancock County Planning Commission was formed by itself with government sanction; members are on salary. Down East Health Services discussed with Mrs. Van Pelt. Dr. Randall Silver is one of the medical directors.

QUINBY D. GURNEE, M.D., *Secretary*

Penobscot

The Annual Meeting of the Penobscot County Medical Society was held on May 16, 1978 at Sing's Restaurant in Bangor. About forty members attended.

The meeting was opened by the President, Dr. Philip Hunter; the minutes of the April meeting were approved. Regarding the unintelligible language of many insurance policies that had been criticized by a letter from Dr. Leonidas at the April meeting, a reply from Dr. Lightbody, who is a member of the Board of Directors of Maine Blue Cross and Blue Shield, indicated that there is both a State and national effort to simplify the language of the insurance policies; however, legally this would allow more latitude in the courts and this aspect of changing the language has been the stumbling block. Correspondence from the Maine Medical Association regarding Senator Hathaway's support of Certificate of Need bills nationally was noted; members of M.M.A. are urged to respond in letter form to Senator Hathaway registering their disapproval of such a view. There was some discussion regarding the Medical Mutual Insurance Company of Maine; President Hunter elaborated on the organization of the company and its planned effective date for writing policies of July 1, 1978. Currently there seems to be some delay in obtaining a license for the company in the Insurance Commissioner's office in Augusta.

Two applications for membership to the County Society were presented: Drs. Thaddeus H. Jozefowicz and Paul A. Liebow; both were unanimously approved.

The Treasurer's report was read. There seems to have been a general increase in the funds of the County Society and there was considerable discussion on a plan to use these funds or reduce the current dues. Dr. Holzwarth made a motion to reduce the dues from the current $40.00 to $30.00 per year; the motion was tabled by Dr. Kittredge, who suggested that the President of the County Society report to the members at the Fall meeting with recommendations regarding the best use of the funds, i.e., reduced dues or investments or charitable contributions.

The report of the Nominating Committee, composed of Drs. Merriam, Woodcock, and Beebe was presented for officers and delegates for the year 1978-79. The entire slate was accepted as presented. The following is the list of officers and delegates for the year 1978-79:

President, Dr. David S. Beebe, Bangor

President-Elect, Dr. H. Clement Jurgeleit, Bangor

Secretary, Dr. James R. Curtis, Bangor

Treasurer, Dr. Michael B. Solomon, Bangor

Counselor (3 yrs.), Dr. William E. Clark, Jr., Bangor

Counselor (1 yr. term to fill out Dr. Schroder's unexpired term), Dr. John J. McDevitt, 4th, Bangor

Delegates to the M.M.A. House of Delegates: Drs. A. Dewey Richards, Orono, H. Clement Jurgeleit, Jack N. Meltzer, John F. Adams, Jr., Parker F. Harris, Thomas L. Watt, and R. Russell Lang, all of Bangor. Alternates: Drs. Richard L. Field, Don L. Maunz, Harry S. Tamm, Donald G. Metzger, Patrick W. Kamm, John S. Kaiser, and Denis F. J. Halmagyi, all of Bangor

The meeting was adjourned at 9:30 p.m.

JAMES R. CURTIS, M.D., *Secretary*

Franklin

The Franklin County Medical Society met on July 10, 1978 at the Franklin County Hospital. The meeting was called to order by the President, Dr. James R. MacMahon.

A report of the action taken by the Maine Medical Association House of Delegates at its June meeting on the several resolutions was discussed at the previous County meeting by Drs. Onion and Fiorica.

Drs. Fiorica and Prior volunteered to participate in the Maine Medical Association's participation in the formulation of the H.S.A. new health plan for the State of Maine.

Dr. MacMahon was named County Society Coordinator for Statewide immunization program activities with the State Medical Association.

A meeting of the Franklin County Medical Society was held at

First year medical resident with three years experience in U.S.A. wishes to do locum tenens for whole month of March 1979 either for General Practice or Emergency Room. Fully licensed in Maine.

Reply to Maine Medical Association, P.O. Box 250, Brunswick, Maine 04011.

the Franklin County Hospital on October 2, 1978. The meeting was called to order by the President, Dr. James R. MacMahon.

Dr. MacMahon announced the willingness of Blue Cross/Blue Shield to come and make a presentation regarding the history of their organization. Franklin County Society, after discussion of the possible times that this might be held, voted to decline with thanks the offer because of the difficulties of scheduling it.

Election of delegates and officers by unanimous ballot. The incumbents were re-elected:

President, Dr. James R. MacMahon, Farmington
Secretary-Treasurer, Dr. Daniel K. Onion, Farmington
Delegate to the M.M.A. House of Delegates: Dr. David S. Hurst, Farmington. Alternate: Dr. Gaetano T. Fiorica

The County voted to have dues of $1.00 for the upcoming year and have the Maine Medical Association bill for it.

DANIEL K. ONION, M.D., *Secretary*

M.M.A. SPECIAL COMMITTEES—1978-1979—*Continued from Page 342*

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HILADELPHIA

APR 21 1978

Supplement to

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April 1978

MEDICAL SPECIALTIES

The following Specialties, including Family Practice, are recognized by the American Medical Association:

A	Allergy (sub-Specialty of Internal Medicine)
AM	Aerospace Medicine (special field of Preventive Medicine)
AN	Anesthesiology
CD	Cardiovascular Diseases (sub-Specialty of Internal Medicine)
CDS	Cardiovascular Surgery
CHP	Child Psychiatry (sub-Specialty of Psychiatry)
CRS	Colon and Rectal Surgery
D	Dermatology
DR	Diagnostic Roentgenology (Special field of Radiology)
EM	Emergency Medicine
END	Endocrinology
FOP	Forensic Pathology (special field of Pathology)
FP	Family Practice
GE	Gastroenterology (sub-Specialty of Internal Medicine)
GPM	General Preventive Medicine (special field of Preventive Medicine)
GS	General Surgery
HEM	Hematology
IM	Internal Medicine
N	Neurology
NEP	Nephrology
NS	Neurological Surgery
OB	Obstetrics
OBG	Obstetrics and Gynecology
OM	Occupational Medicine (special field of Preventive Medicine)
ONCO	Oncology
OPH	Ophthalmology
ORS	Orthopedic Surgery
OTO	Otorhinolaryngology, Otolaryngology
P	Psychiatry
PD	Pediatrics
PDA	Pediatric Allergy (sub-Specialty of Pediatrics)
PDC	Pediatric Cardiology (sub-Specialty of Pediatrics)
PDNEP	Pediatric Nephrology
PDS	Pediatric Surgery
PH	Public Health (special field of Preventive Medicine)
PM	Physical Medicine and Rehabilitation
PS	Plastic Surgery
PTH	Pathology
PUD	Pulmonary Diseases (sub-Specialty of Internal Medicine)
R	Radiology
RHU	Rheumatology
TR	Therapeutic Radiology (special field of Radiology)
TS	Thoracic Surgery
U	Urology
VS	Vascular Surgery
00	Unspecified (retired, not in practice, no specialty reported)
99	Other

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Cheng, Hsueh-ching (IM)	12 Spruce St., Augusta 043
Cho, Sung W. (IM)	150 Dresden Ave., Gardiner 043
Ciembroniewicz, Julius E. (NS,N)	15 Middle St., Augusta 043
Clarke, Daniel B. (D)	12 Spruce St., Augusta 043
Collins, H. Douglas (IM)	12 E. Chestnut St., Augusta 043
Coyne, Nancy M. (P)	Rt. 1, Stanley Hill Rd., North Vassalboro 049
Crawford, Joseph R. (FP,GS)	12 Spruce St., Augusta 043
Cruickshank, Frank S., Jr. (R)	Eaton Dr., Waterville 049
Culver, Raymond E. (IM,GE)	325 Kennedy Mem. Dr., Waterville 049
Dachslager, Philip (FP,IM)	72 Winthrop St., Augusta 043
Darlington, Brinton T. (IM)	32 Westwood Rd., Augusta 043
Davis, Earle M. (U)	325 Kennedy Mem. Dr., Waterville 049
Davis, George E., Jr. (IM,GE)	12 Spruce St., Augusta 043
Day, Robert B. (ORS)	75 Stone St., Augusta 043
deFreitas, Andre M. (P)	19 Cushnoe Dr., Augusta 043
Dela Cruz, Teodoro C. (N,NS)	15 Middle St., Augusta 043
Denison, John D. (P.A.)-FP	89 Hospital St., Augusta 043
Dennis, Richard H. (OPH)	325 Kennedy Mem. Dr., Waterville 049
Diehl, William H., Jr. (OTO)	325B Kennedy Mem. Dr., Waterville 049
Dole, Richard R. (IM)	325 Kennedy Mem. Dr., Waterville 049
Dore, Clarence E. (FP)	2 School St., Waterville 049
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Guite, L. Armand, Jr. (GS)	325B Kennedy Mem. Dr., Waterville 049
Halperin, David C. (GS)	89 Hospital St., Augusta 043
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Hill, Anthony B. (IM)	258 Main St., Saco 040
Hill, Kevin (OPH)	325A Kennedy Mem. Dr., Waterville 049
Hornberger, H. Richard (P.A.)-(TS,GS)	325 Kennedy Dr., Waterville 049
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Ross, Stephen A. (IM,HEM,ONCO) Penob. Bay Physicians' Bldg., Glen Cove, Rockland 04841
Schoon, David L. (RD) Penob. Bay Physicians' Bldg., Glen Cove, Rockland 04841
Shrier, Peter R. (OBG) Rt. 1, Glen Cove 04846
Sigafoos, J. Harvey (AN) Pleasant Point 04563
Sube, Janis (GS) 108 Elm St., Camden 04843
Ward, William W. (GS,99) Box 646, Rockland 04841
Warren, Henry S. (FP) Derby Rd., Islesboro 04848
Wasgatt, Wesley N. (FP) 41 Talbot Ave., Rockland 04841
Waterman, Dorothy (FP) Waldoboro 04572
Waterman, Richard (FP) Main St., Waldoboro 04572
Weaver, Donald J. (IM) 121 Main St., Thomaston 04861
White, Henry O. (P.A.)-(GS) Penob. Bay Physicians' Bldg., Glen Cove, Rockland 04841
Wickenden, John W. (ORS) Penob. Bay Physicians' Bldg., Glen Cove, Rockland 04841

Wickenden, Roger W. (ORS)	Penob. Bay Physicians' Bldg., Glen Cove, Rockland 04841
Williams, John G., Jr. (FP)	P.O. Box 95, Glen Cove 04846
Williams, Thomas W. (P.A.)-(IM)	Penob. Bay Physicians' Bldg., Glen Cove, Rockland 04841
Worthing, Verla E. (AN)	199 Main St., Thomaston 04861

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Apollonio, Howard L. (OO) (Retired)	Box 34, Rockport 04856
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Naumer, Harry A. (OO)	Lands End, Port Clyde 04855
Saunders, Sallie H. (00) (Retired)	Star Route, Lincolnville 04849
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Ashley, Alta (FP) (Retired)	Box 87, Monhegan 04852
Giustra, Frank X. (PD)	6 Eaton Ave., Camden 04843
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Tounge, Harry G., Jr. (FP)	12 Union St., Camden 04843

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Dennison, Frederick C. (IM) (Retired)	3 Gillchrest St., Thomaston 04861
Stroud, Geoffrey A. (FP)	65 Baribeau Dr., Brunswick 04011

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Avantaggio, Frank O., Jr. (GS)	Bristol Rd., Damariscotta 04543
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Bullington, Sunny J. (OPH)	1143 Washington St., Bath 04530
Burden, Charles E. (PD)	1 North St., Bath 04530
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Cunningham, Alice N. (OBG)	Parkview Professional Bldg., Brunswick 04011
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Dominici, Raymond H. (GS,Ind.Med.)	4 Park St., Bath 04530
Dumdey, Paul H. (IM)	6 Oak Grove Ave., Bath 04530
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Evans, Richard III (P)	56 Baribeau Dr., Brunswick 04011
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Haughwout, Peter J. (OTO)	66 Baribeau Dr., Brunswick 04011
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Hill, David S. (FP)	10 Oak Grove Ave., Bath 04530
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Keating, Anthony J. (FP)	10 Oak Grove Ave., Bath 04530
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Burke, Paul W. (FP)	5 High St., Newport 04953
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Gilladoga, Angela C. (PD)	417 State St., Bangor 04401
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An Alphabetical List of the Members of the Maine Medical Association

The figures in parentheses refer to County Societies as follows: (1) Androscoggin, (2) Aroostook, (3) Cumberland, (4) Franklin, (5) Hancock, (6) Kennebec, (7) Knox, (8) Lincoln-Sagadahoc, (9) Oxford, (10) Penobscot, (11) Piscataquis, (12) Somerset, (13) Waldo, (14) Washington, (15) York.

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Chase, Barbara A., 618 Main St., Lewiston 04240 (1)
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Collins, Thomas M., P.O. Box 71, Sanford 04073 (15)
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Cousineau, Leo E., 10 High St., Lewiston 04240 (1)
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Mitchell, Hazen C., Calais 04619 (14)
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***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**
Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies Observe usual precautions in impaired renal or hepatic function Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation
Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported, should these occur, discontinue drug Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy

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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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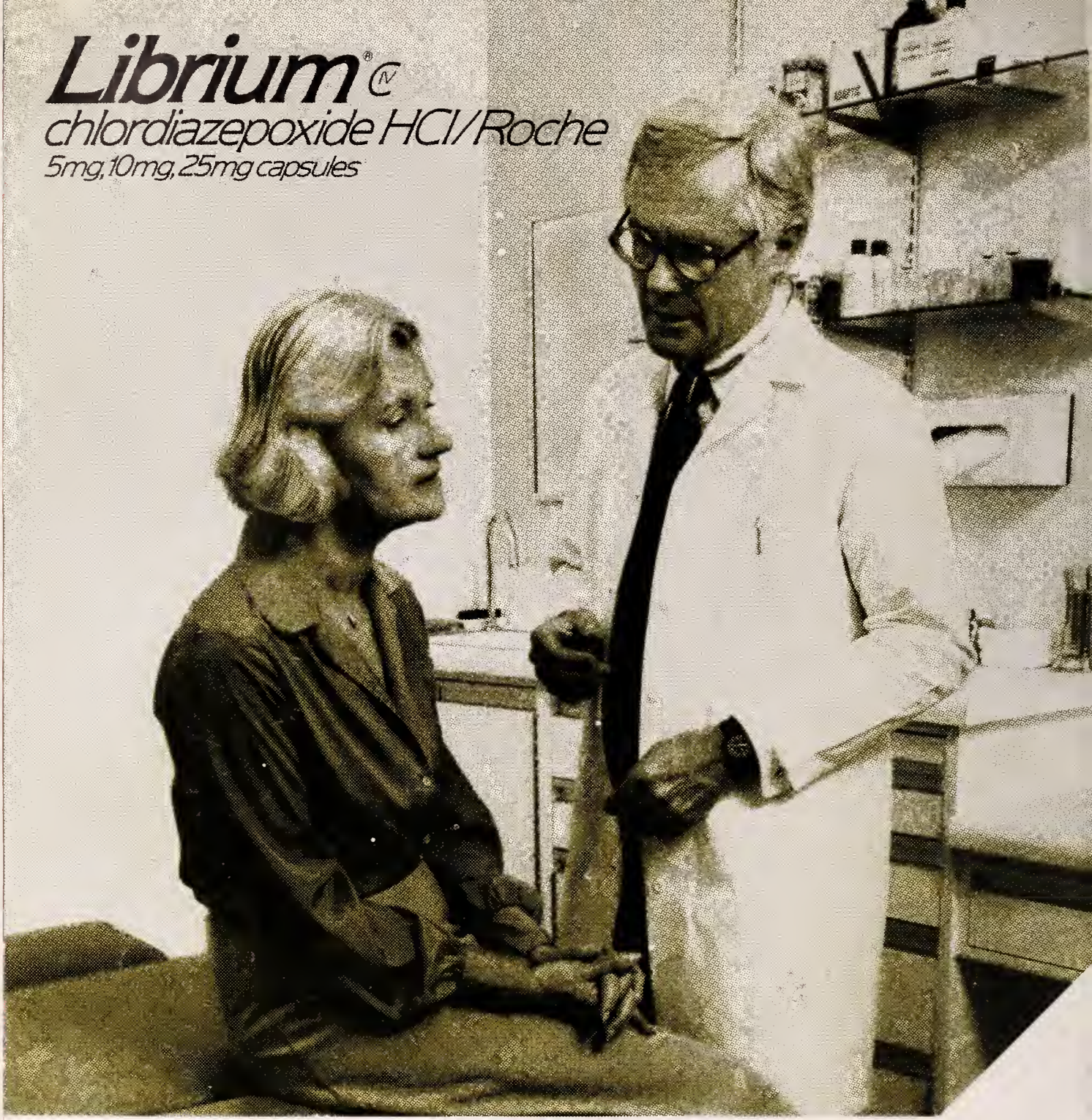
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